

**PATIENT AND TREATMENT RELATED  
FACTORS RESPONSIBLE FOR RADIATION  
PNEUMONITIS IN POSTMASTECTOMY  
RADIATION AND THE IMPACT OF  
SUPRACLAVICULAR RADIATION**



A dissertation submitted to

The Tamil Nadu Dr. M.G.R. Medical University, Chennai,

In partial fulfilment of the requirements for the award of

The degree of

**DOCTOR OF MEDICINE (M.D.) IN RADIOTHERAPY**

**APRIL 2018**

## CERTIFICATE

This is to certify that this dissertation titled, **“PATIENT AND TREATMENT RELATED FACTORS RESPONSIBLE FOR RADIATION PNEUMONITIS IN POSTMASTECTOMY RADIATION AND THE IMPACT OF SUPRACLAVICULAR RADIATION.”** is a bonafide record of the work done by Dr. Anupama Reddy P.S, in the Division of Radiation Oncology, Cancer Institute (W. I. A.), Chennai, during the period of her postgraduate study for the degree of M.D. (Branch IX – Radiotherapy) from 2015-2018 under my direct guidance and supervision.

Date:

Dr.G.Selvaluxmy,

Place: Chennai

Professor and Head of

Department,

Division of radiation oncology,

Cancer institute, (WIA), Chennai

## **ACKNOWLEDGMENT**

The common practice at the Institute was to treat breast cancer patients with 4 or more positive nodes with post mastectomy Loco regional radiotherapy LRRT. Today all node positive patients irrespective of the number of nodes involved are considered for LRRT, which includes chest wall radiation along with internal mammary, infra-clavicular and supraclavicular nodal irradiation. The purpose of my study is to analyse the toxicity to lung following loco regional radiation and the impact of regional nodal irradiation especially supraclavicular radiation and its association with Radiation Pneumonitis. I would like to acknowledge my sincere gratitude to late Dr.S.Krishnamurthy, advisor and Dr.V.Shanta, executive chairman, Cancer institute (WIA) for providing me the opportunity to carry out this study.

I am grateful to Prof. Dr. Selvaluxmy, Professor, Head of the department of Radiation oncology, Additional director, Cancer Institute for her continued encouragement and invaluable suggestions during this study. Without her this study would not have been possible.

I thank Dr R.Swaminathan, Head of Department Epidemiology, Assistant Director Cancer Institute for helping me with the data analysis.

I sincerely thank Dr. Ananthi Balasubrahmanian, Associate Professor, Department of Radiation oncology who guided me and helped me complete the study. I thank Dr.Priya Iyer, Associate professor, Department of radiation oncology for her constant inputs. I also thank Dr Shiva Subrahmanian radiologist and Mr Sam Devakumar, Physist, who cleared my doubts and gave ideas for the study.

I thank my Parents, Dr Uddaya Shrie, Advocate & Astrologer and Sri Krishna Reddy, Medical physist for putting me in this field of medicine and for their unending support and encouragement.

I thank all my teachers who were always the source of motivation. I express my gratitude to all my colleagues and all staff in radiotherapy and tumor registry department who were unfailing in extending their support.

I am ever thankful to all patients who were a part of this study, and pray for their speedy recovery. I thank Almighty, whose love on me, helped me to respect others love and to love all equally.



# CANCER INSTITUTE (W.I.A)

(REGIONAL CANCER CENTRE)  
INSTITUTIONAL ETHICS COMMITTEE

Reg. No. ECR/235/Inst/TN/2013

Adyar, Chennai - 600 020.

Phone : 044-22209150 Extn : 129, Fax : 044-22354508

E-mail : [iec@cancerinstitutewia.org](mailto:iec@cancerinstitutewia.org)



Date :

Ethics Committee Re-Registration No.ECR/235/Inst/TN/2013/RR-16

5 September 2017

To,  
Dr. Anupama Reddy  
Resident  
Dept. of Radiation Oncology  
Cancer Institute (W.I.A)  
38, Sardar Patel Road  
Chennai 600 036

**Subject: Ethics Committee Approval Letter**

**Reference: Study Protocol titled "Patient and treatment related factors responsible for Radiation Pneumonitis in post mastectomy radiation and the impact of supraclavicular radiation".**

Dear Dr. Anupama,

This is with reference to the letter dated 14 July 2017 for review of the above referenced study Protocol. The ethics committee reviewed the following documents.

- 1) Study Protocol
- 2) Study Synopsis
- 3) Letter of Undertaking

The following members of the ethics committee were present at the ethics committee meeting held on 22.07.2017 at 2.00 pm at auditorium, 1<sup>st</sup> Floor, Bhagwan Adinath Jain Complex, Dr. Krishna Murthy Campus, Cancer Institute (W.I.A), Chennai 600 036.

S. No	Name	Role/ Designation in ethics committee	Affiliation of the member with Institution	Attendance to the meeting 22.07.2017
1	Dr. V.I. Mathan	Chairman	Not affiliated with Cancer Institute	Present
2	Dr. T.G. Sagar	Member Secretary	Affiliated with Cancer Institute	Present
3	Dr.G.Selvaluxmy	Clinician	Affiliated with Cancer Institute	Present
4	Dr.K.Kalai Chelvi	Clinician	Not affiliated with Cancer Institute	Present
5	Dr.V. Sridevi	Clinician	Affiliated with Cancer Institute	Present
6	Dr.V.K. Ramadesikan	Basic Medical Scientist	Not affiliated with Cancer Institute	Present
7	Mrs.Ranganayaki Kumar	Lay Person	Not affiliated with Cancer Institute	Present
8	Mr. M. Suresh	Legal Expert	Not affiliated with Cancer Institute	Present
9	Dr. S. Padma	Legal Expert	Not affiliated with Cancer Institute	Present
10	Mr. Chaganti V. K. Maitreya	Social Scientist	Not affiliated with Cancer Institute	Present
11	Dr.Niranjali Devaraj	Scientific Member	Not affiliated with Cancer Institute	Present

The Institutional Ethics Committee, Cancer Institute (W.I.A) functions in accordance with Ethical Guidelines for Bio-Medical Research on Human Participants issued by ICMR, Schedule Y of Drugs and Cosmetics Act 1940 and Rules 1945 and Indian Good Clinical Practice Guidelines.



# CANCER INSTITUTE (W.I.A)

(REGIONAL CANCER CENTRE)  
INSTITUTIONAL ETHICS COMMITTEE

Reg. No. ECR/235/Inst/TN/2013  
Adyar, Chennai - 600 020.

Phone : 044-22209150 Extn : 129, Fax : 044-22354508  
E-mail : [iec@cancerinstitutewia.org](mailto:iec@cancerinstitutewia.org)



Date :

The above documents were reviewed and the study was approved by the ethics committee to be conducted in its presented form in accordance with applicable regulations.

Yours Sincerely,

**Dr. T.G. Sagar**  
**Member Secretary**  
**Institutional Ethics Committee**





## Urkund Analysis Result

**Analysed Document:** Thesis for printing.docx (D31388731)  
**Submitted:** 10/17/2017 8:29:00 AM  
**Submitted By:** subrahmanyaanupama@gmail.com  
**Significance:** 3 %

### Sources included in the report:

Thesis copy final1.docx (D31184787)  
Thesis copy semifinal.docx (D30605160)  
document.docx (D31094923)  
Comparative study of neoadjuvant chemotherapy in hormone receptor positive and negative locally advanced breast carcinoma.docx (D30755485)  
document.docx (D31094971)  
document.docx (D31059655)  
Comparative study of neoadjuvant chemotherapy in hormone receptor positive and negative locally advanced breast carcinoma.docx (D30753575)  
THESIS Final sony.docx (D30753015)  
FASTING INSULIN LEVELS IN NON DIABETIC final.docx (D31337776)

### Instances where selected sources appear:

## **ABSTRACT**

### **PATIENT AND TREATMENT RELATED FACTORS RESPONSIBLE FOR RADIATION PNEUMONITIS IN POSTMASTECTOMY RADIATION AND THE IMPACT OF SUPRACLAVICULAR RADIATION**

**Dr. Anupama Reddy P.S, Cancer institute (WIA)**

#### **Aim:**

To Study the incidence of symptomatic and radiological pneumonitis in patients receiving post mastectomy loco regional radiation.

#### **Materials and Methods:**

Retrospective analysis of 152 patients treated with adjuvant post-mastectomy radiation from January 2015 to August 2016 was done. All patients received loco-regional radiation using single iso-centric photon three-dimensional conformal radiation to a total dose of 4680cGy. Two plans with and without addition of supraclavicular (SCL) region were also generated for 30 patients and Dose volume histogram (DVH) parameters including lung volume and Mean Lung Dose (MLD) for all patients were analysed. Chest radiographs done prior and one year after completion of radiation were reviewed for radiation pneumonitis and scored as per Modified WHO Grading System for Radiographic Pulmonary Toxicity (RPT). Other patient related parameters like age, side of treatment, comorbid illness, chemotherapy and hormonal therapy details were noted.



**Results:**

At a median follow up of 21 months, none had symptomatic pneumonitis. At 1 year of completion of radiation 26 patients developed RPT (17.1%). The average MLD with and without SCL is 14.9Gy and 13.5Gy respectively. 24 developed RP in tangential field territory and 2 developed in SCL territory. Increased age was significantly associated with development ( $P<0.001$ ) and severity ( $P=0.083$ ) of RPT. Patients irradiated on Right side were less associated with RPT ( $p=0.037$ ), RPT was more commonly associated with patients exposed to Tobacco/passive smoking ( $p<0.001$ ) and bronchial asthma ( $p=0.012$ ). With a lung constraint of  $V20<30\%$  and  $MLD<15\text{ Gy}$  none of the DVH parameters was associated with development of RPT. CMF chemotherapy ( $p=0.06$ ) and Aromatase inhibitors-Letrozole ( $p=0.05$ ) were associated with increased development of RPT which may be due to the elderly group of patients receiving these therapies.

**Conclusion:**

There was no symptomatic pneumonitis and incidence of Radiation Pulmonary toxicity was only 17.1%. It was observed that  $\text{age}>50\text{years}$  was a significant factor for development of RPT. Other factors like bronchial asthma, exposure to passive smoking and irradiation of left side are also associated with development of RPT. Addition of regional radiation did not increase RPT. Prospective studies are required as consensus guidelines regarding factors responsible for radiation pneumonitis are not available.

**Key words:**

Breast cancer, Post mastectomy Locoregional radiotherapy, Radiation pneumonitis.

## **TABLE OF CONTENTS**

<b>SNo</b>		<b>Heading</b>	<b>Pg No</b>
<b>I</b>		<b>Introduction</b>	<b>1-43</b>
	1.1	Breast Anatomy, Development and Pathology	1-12
	1.2	Breast cancer Staging, Epidemiology	13-18
	1.3	Role of surgery in breast cancer	19-21
	1.4	Role of chemotherapy in breast cancer	22-25
	1.5	Role of hormonal therapy in breast cancer	26-30
	1.6	Role of radiotherapy in breast cancer and post mastectomy radiotherapy	31-34
	1.7	Radiobiology of lungs and Radiation pneumonitis	34-38
	1.8	Review of literature	39-43
<b>II</b>		<b>Objectives and methodology</b>	<b>44-58</b>
	2.1	Aim	44
	2.2	Objectives	44-45
	2.3	Patients and methods.	45-58
<b>III</b>		<b>Results and Statistical analysis</b>	<b>59-83</b>
<b>IV</b>		<b>Discussion</b>	<b>84-89</b>
<b>V</b>		<b>Conclusion</b>	<b>90</b>
<b>VI</b>		<b>Reference</b>	<b>91-96</b>

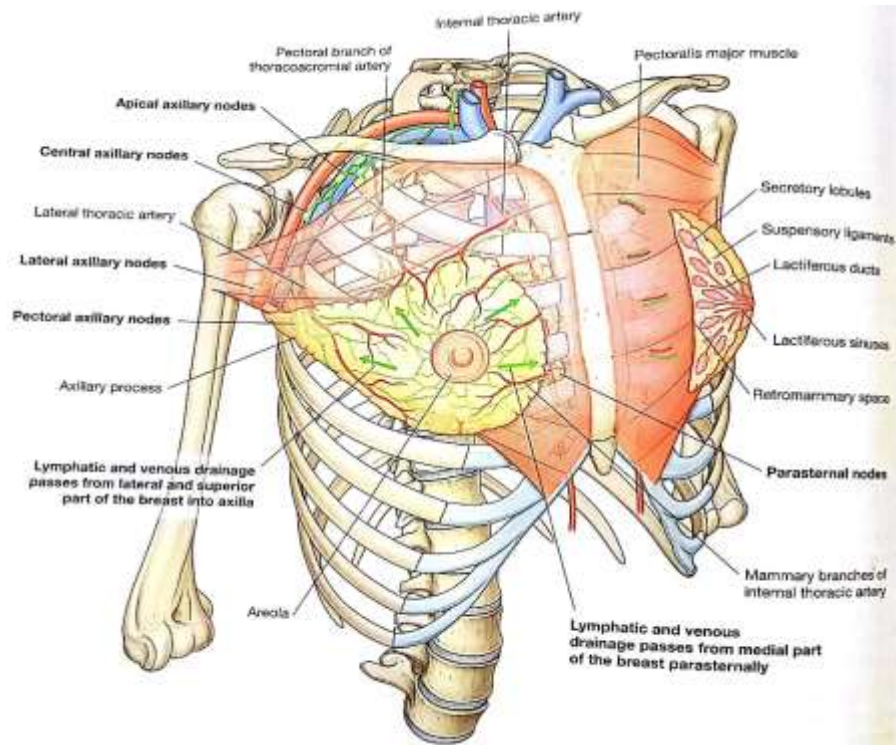
## **I. INTRODUCTION**

### **1.1.a ANATOMY:**

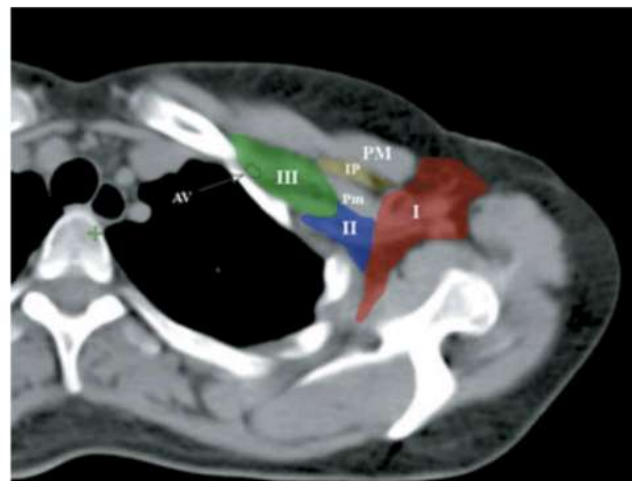
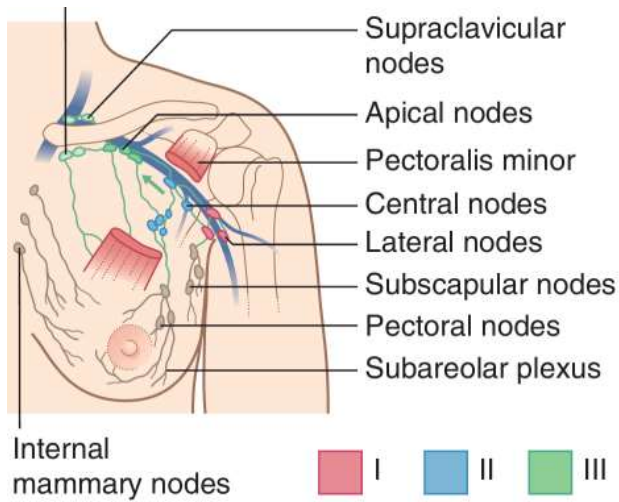
Breasts are modified skin appendages that provide complete nourishment and immunologic protection for the young. They are paired mammary glands that rest on the pectoralis muscle on the upper chest wall. They are composed of specialized epithelium and stroma that give rise to benign and malignant lesions specific to the organ.

#### **Pectoral region:**

The pectoral region consists of structures external to anterior chest wall. It is divided into superficial compartment (Skin, Superficial fascia, Breasts) and deep compartment (muscles and associated structures). Each breast extends horizontally from midline to mid axillary line laterally, vertically from 2<sup>nd</sup> rib superiorly to 6<sup>th</sup> rib inferiorly, externally the inferior border is the infra mammary crease. For describing the position of lesions each breast is divided into 4 Quadrants (Upper outer, Upper Inner, Lower outer, Lower inner) central sector and axillary tail of Spence. Greater percentage of cancers are seen in UOQ.



**Fig 1: Anatomy of Breast**



**Fig 2: Regional lymph nodes a) Schematic view b) Delineated on a CT axial view**

## **Lymphatic Drainage:**

- Axillary lymph nodes

Level I- Caudal and lateral to pectoralis minor muscle (Low axillary group)

Level II- Beneath pectoralis minor muscle (Mid axillary group)

Level III- Cranial and medial to pectoralis minor muscle (High axillary/ Apical/ Infra clavicular group)

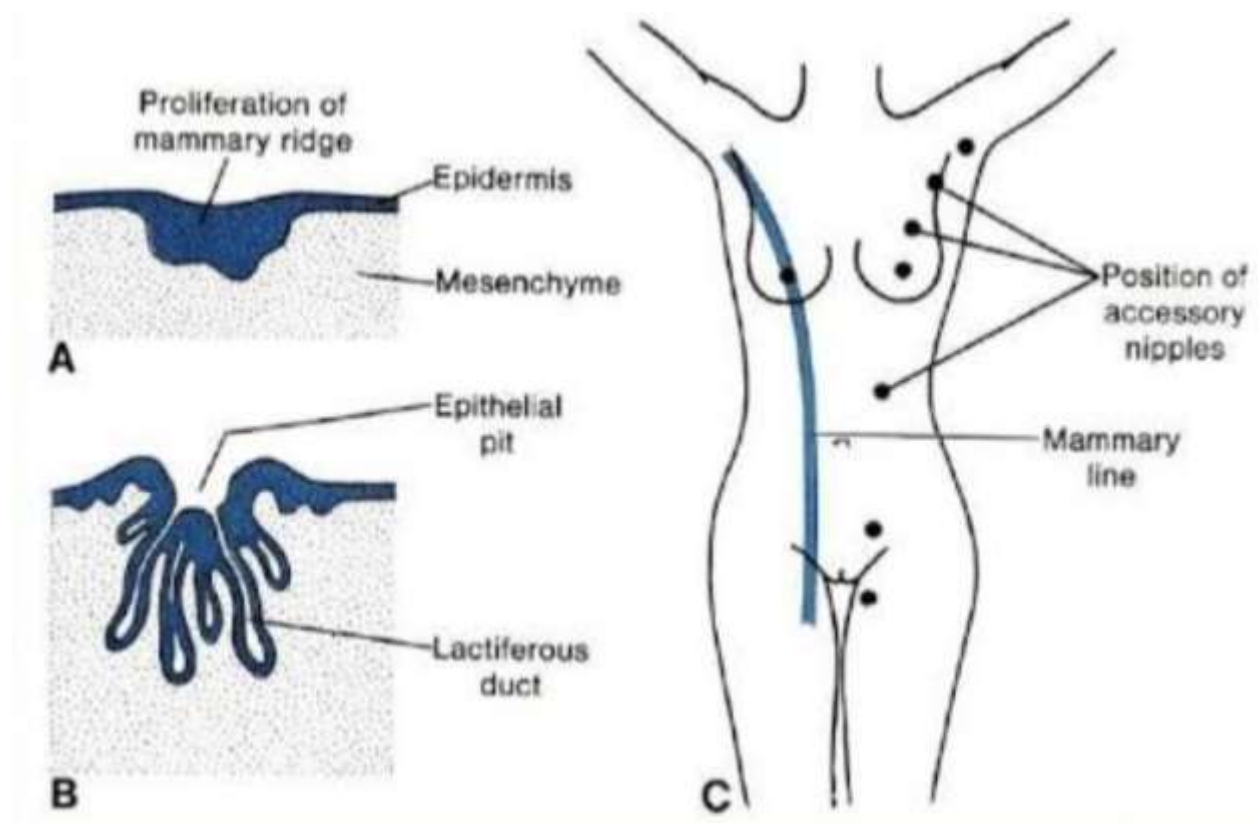
- Supra clavicular lymph nodes (SCL)
- Internal mammary lymph nodes (IMR) - 3 to 4 cm lateral to midline in first three intercostal spaces along internal mammary artery and vein

### **1.1.b DEVELOPMENT**

In embryonic stage mammary glands first appear as elevated ridges along milk line. Milk lines or milk Ridges (mammary ridge) are two lines formed by thickening of epidermis along the ventral surface of mammals of both sexes. They extend from axilla to perineum. They then separate into individual buds located in regions lateral to ventral midline.

In humans milk line appears in 7<sup>th</sup> week of embryonic development. After initial development they go into remission. They may aberrantly form

supernumerary nipples (Polythelia). 6 to 10 major ductal systems originate at the nipple. The keratinizing squamous epithelium of the overlying skin continues into ducts and then abruptly changes to a double layered cuboidal epithelium. A small keratin plug is often found at the orifice of duct. The surrounding areolar skin is pigmented and supported by smooth muscle. Successive branching of large ducts eventually leads to terminal duct lobular unit (TDLU). In women terminal duct branches into a grape like clusters of small acini to form a lobule. Sometimes ducts extend into subcutaneous tissue/ chest wall/ axilla- accessory breast.



**Fig 3: Development of breast**



## ***LIFE CYCLE CHANGES***

Breast is not fully formed at birth. It undergoes cyclical changes during reproductive life. It starts to involute long before menopause.

- Mid embryogenesis - specialised mesenchyme of the breast fat pad condenses around the epithelium of the breast bud. Epithelial cells invade stroma to form rudimentary ducts
- Pre pubertal breast - in male and females consists of large duct system ending in terminal ducts with minimal lobules
- Beginning of menarche- in females terminal ducts give rise to lobules and inter lobular stroma increases in volume. There is paucity of adipose tissue – therefore pubertal breast is radio-dense
- Follicular phase- lobules are relatively quiescent. After ovulation, under the influence of oestrogen and rising progesterone, cell proliferation increases, number of acini per lobule increases with vacuolization of epithelial cells and intra lobular stroma becomes oedematous causing fullness. During menstruation, there is fall in estrogen and progesterone, which causes epithelial cell apoptosis, disappearance of stromal edema and regression of size of lobules.
- Pregnancy- complete morphological maturation and functional activity is seen. Lobules increase in size and number. End of pregnancy breast is

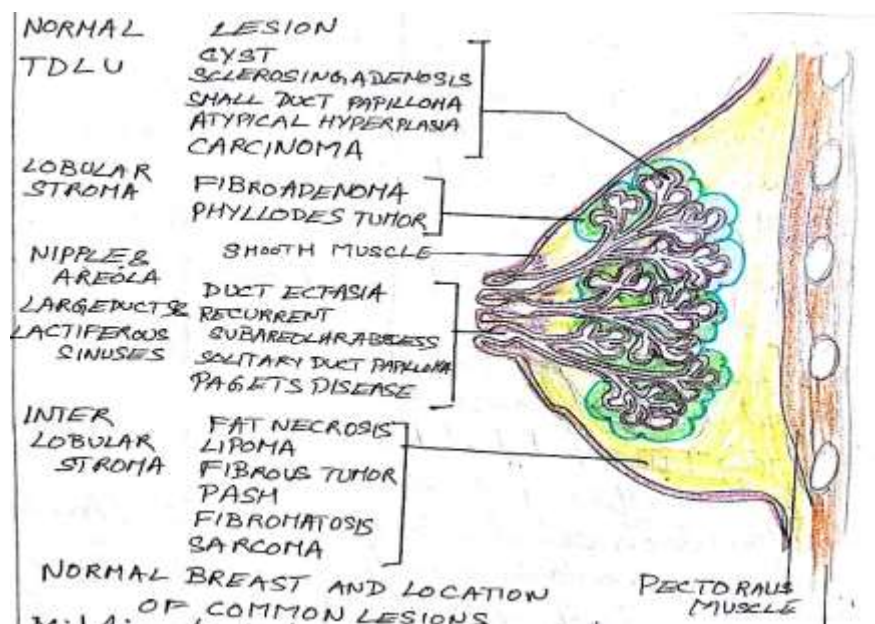
composed almost entirely of lobules separated by a relatively scant amount of stroma. Numerous dermal glands in areola form Montgomery tubercles needed for nipple lubrication. Epithelial cells of TDLU – secretory vacuoles of lipid material are present but milk production is inhibited by high level of progesterone. Immediately after child birth – breast produces colostrum (High in protein) which changes to milk (High in fat and calories) with in first 10 days as progesterone levels drop.

- After cessation of lactation- lobules regress and atrophy, total breast size diminishes markedly. Complete regression to normal nulliparous breast does not occur and there is a permanent increase in size and number of lobules.
- After 3<sup>rd</sup> decade- lobules and their specialised stroma start to involute. The lobules may almost totally disappear leaving only ducts similar to male breast. The radio dense fibrous stroma (inter lobular) is replaced by radiolucent adipose tissue

## HISTOLOGY

Breasts consist of

- 1) Ducts and lobules-lined by 2 cell types, committed stem cells gives rise to both
  - a) Myoepithelial cells- flattened discontinuous layer of contractile cells containing myofilaments lying on basement membrane – responsible for milk ejection.
  - b) Luminal cells – line the lumen- produce milk, except in large ducts.
- 2) Inter lobular stroma – dense fibrous connective tissue mixed with adipose tissue
- 3) Intra lobular stroma – breast specific, hormonally responsive, delicate, myxomatous stroma with scattered lymphocytes



**Fig 4: Breast tissue and associated pathology**

### **1.1.c PATHOLOGY**

#### ***BENIGN EPITHELIAL LESIONS***

##### **Non proliferative breast changes-**

##### Fibrocystic changes (FCC)

Clinically Lumpy bumpy breast

Radiological Dense breast with cysts

Pathology benign morphologic changes

Cysts are formed by the coalescence of the dilated and unfolded ducts and lobules.

Fibrosis occurs due to release of secretory material into adjacent stroma resulting in chronic inflammation and fibrous scarring.

Adenosis is due to increase in number of acini per lobule

##### **Proliferative breast disease without atypia**

Clinically rarely form palpable mass, detected as mammographic densities, Proliferation of ductal epithelium/stroma without cellular abnormalities. These include the following-

Epithelial hyperplasia more than 2 cell layers (luminal & myoepithelial) florid > 4 cell layers.

Sclerosing adenosis No of acini per terminal duct is increased to at least twice the number found in uninvolved lobules

Complex sclerosing lesion (Radial scar)

Papillomas- multiple branching fibro vascular cores. Connective tissue axis lined by luminal and myo-epithelial cells.

Large duct papillomas- multiple and situated deeper with in the ductal system. Increased risk of carcinoma.

Fibro adenoma with complex features

### **Proliferative breast disease with atypia**

Atypical ductal hyperplasia- (ADH) histologic resemblance to DCIS monomorphic cell population regular cell placement around lumina but limited in extent and fail to fill ductal space.

Atypical lobular hyperplasia- (ALH) identical to LCIS, but cells do not fill or distend more than 50% of acini with in the lobule. ALH extending to ducts is associated with increased risk of developing invasive carcinoma.

Atypical hyperplasia is a cellular proliferation resembling DCIS/LCIS but lacking qualitative /quantitative features to diagnose carcinoma in situ

Lobular carcinoma in situ- (LCIS) Incidental finding in a biopsy done for other reasons. Not associated with calcification / stromal reaction- density. More common in young women prior to menopause; B/L in 20-40%. Morphology ALH/LCIS/Lobular carcinoma. Small cells with oval/round nuclei with small nucleoli that do not adhere to one another. Signet ring cells containing mucin are commonly present. Usually ER/PR positive Her 2 neu over expression not observed. Multicentric and bilateral. In may transform to invasive carcinoma in 25-35 % patients after 20 years. The annual risk of transformation is 1%. Ipsilateral breast may be at greater risk. Treatment options include bilateral prophylactic mastectomy, Tamoxifen, Close clinical FU and mammographic screening. LCIS is not true neoplasm. It is a marker of breast cancer risk. Loss of heterogeneity on chromosome 16 q, the location of gene for e cadherin, a trans-membrane protein responsible for epithelial cell adhesion, is lost.

## ***CARCINOMA IN SITU***

### **Ductal Carcinoma In Situ (DCIS)**

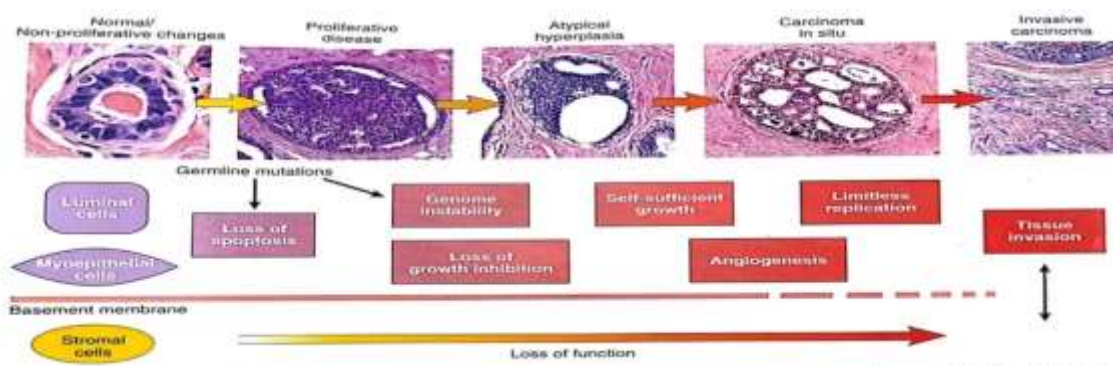
15-30% carcinomas in well screened populations, Among mamographically detected cancers half are DCIS. Mammographic calcifications occur. Malignant cells are limited to ducts and lobules by basement membrane. Myoepithelial cells are preserved. Types- Comedo and non comedo (Cribriform, Solid, Papillary,



Micropapillary). Treatment includes Mastectomy. It is curative in 95%. Recurrence occurs if there is residual DCIS in ducts or subcutaneous adipose tissue or there is an occult focus of invasion. Breast conservation surgery is an option and patients with Intermediate and high risk factors for recurrence - Grade, Size, Margins and Age (Van Nuys Prognostic Index) benefit from radiation.

### Pagets Disease of Nipple

Present as unilateral erythematous lesion with scaly crusts over nipple areola complex. Pruritus is common and might be mistaken as eczema. Paget cells extend from DCIS within ductal system into nipple skin without crossing basement membrane. Tumor cells disrupt the normal epithelial barrier therefore extra cellular fluid seeps onto nipple surface. Paget cells are easily detected in exudate cytology/nipple biopsy. Usually poorly differentiated and over express Her2neu. Keratinocytes produce heregulin alpha, which acts via Her2neu receptors and plays a role in pathogenesis.



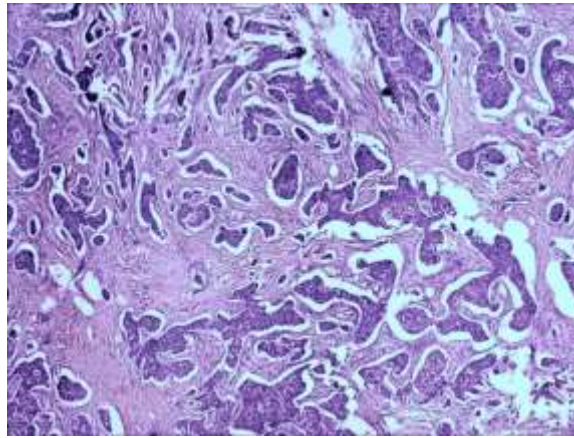
**Fig 5: Pathology of Breast**

## ***INVASIVE CARCINOMA***

### **i) Invasive Carcinoma No Special Type/ Not otherwise specified.**

#### **(NST/NOS)- Infiltrating Ductal carcinoma (70-80 %)**

Firm to hard irregular bordered with pinpoint foci of chalky white elastotic stroma and occasional calcification. Carcinoma of NST are accompanied by varying amount of DCIS



**Fig 6: Invasive Ductal carcinoma**

Well differentiated tubules with hormone receptors and no her2neu over expression. Anastomosing sheets of pleomorphic cells less likely express hormone receptors and more likely Her2neu over expression.

### **ii) Specified/Special type Invasive carcinoma**

Invasive Lobular, Medullary, Mucinous, Invasive papillary, Metaplastic carcinoma

***STROMAL TUMORS*** i) Fibroadenoma, ii) Phylloids, iii) Sarcoma

## **1.2.a STAGING**

### **Definitions of AJCC TNM**

Definition of Primary tumor (T) Clinical and pathological

<b>T category</b>	<b>T criteria</b>
<b>Tx</b>	Primary tumor cannot be assessed
<b>T0</b>	No evidence of primary tumor
<b>Tis (DCIS)</b>	Ductal carcinoma in situ
<b>Tis(Pagets)</b>	Pagets disease of the nipple NOT associated with invasive carcinoma and/or carcinoma in situ (DCIS) in the underlying breast parenchyma.
<b>T1</b>	Tumor $\leq$ 20 mm in greatest dimension
<b>T1mi</b>	Tumor $\leq$ 1 mm in greatest dimension
<b>T1a</b>	Tumor $>$ 1mm but $\leq$ 5 mm in greastest dimension (round any lesion 1.0-1.9 mm to 2 mm)
<b>T1b</b>	Tumor $>$ 5 mm but $\leq$ 10 mm in greatest dimension
<b>T1c</b>	Tumor $>$ 10 mm but $\leq$ 20 mm in greatest dimension
<b>T2</b>	Tumor $>$ 20 mm but $\leq$ 50 mm in greatest dimension
<b>T3</b>	Tumor $>$ 50 mm in greatest dimension
<b>T4</b>	Tumor of any size with direct extension to chest wall and/ or to the skin (ulceration or macroscopic nodule), invasion of the dermis alone does not qualify as T4
<b>T4a</b>	Extension to the chest wall, invasion or adherence to pectoralis muscle in the absence of invasion of chest wall structures does not qualify as T4
<b>T4b</b>	Ulceration and/or ipsilateral macroscopic satellite nodules and/or edema (including peau d' orange) of the skin that does not meet the criteria of inflammatory carcinoma
<b>T4c</b>	Both T4a and T4b are present
<b>T4d</b>	Inflammatory carcinoma

- 1) Carcinoma in the breast parenchyma associated with pagets disease are categorised based on the size and charecteristics of the parenchymal disease, although the presence of pagets disease should still be noted.
- 2) Lobular carcinoma in situ (LCIS) is a benign entity and is removed from TNM staging in the AJCC cancer staging Manual, 8<sup>th</sup> Edition

#### Definition of Regional lymph nodes- Clinical(c N)

<b>cN</b>	<b>cN Criteria</b>
<b>Category</b>	
<b>CNx</b>	Regional lymph nodes cannot be assessed (e.g., previously removed)
<b>cN0</b>	No regional lymph node metastases ( by imaging or clinical examination)
<b>cN1</b>	Metastases to movable ipsilateral Level I,II axillary lymph node(s)
<b>cN1mi</b>	Micrometastases (approximately 200 cells, larger than 0.2 mm, but none larger than 2 mm)
<b>cN2</b>	Metastases in ipsilateral Level I,II axillary lymph nodes that are fixed or matted, or in ipsilateral internal mammary nodes in the absence of axillary lymph node metastases
<b>cN2a</b>	Metastases in ipsilateral Level I,II axillary lymph nodes fixed to one another (matted) or to other structures
<b>cN2b</b>	Metastases only in ipsilateral internal mammary node in the absence of axillary lymph node metastases
<b>cN3</b>	Metastases in ipsilateral infra clavicular (Level III axillary) lymph node(s) with or without Level I, II axillary lymph node involvement, Or in ipsilateral internal mammary lymph node(s) with level I,II axillary lymph node metastases, Or metastases in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement
<b>cN3a</b>	Metastases in ipsilateral infra clavicular (Level III axillary) lymph node(s)
<b>cN3b</b>	Metastases in ipsilateral internal mammary lymph node(s) and axillary lymph node metastases,
<b>cN3c</b>	Metastases in ipsilateral supraclavicular lymph node(s)

- 1) (sn) and (f) suffixes should be added to the N category to denote confirmation of metastasis by sentinel node biopsy or fine needle aspiration/core needle biopsy respectively
- 2) cNx – regional lymph nodes are surgically removed previously / No documentation of physical examination of axilla
- 3) cN1mi- Sentinel lymph node biopsy is performed before tumor resection, (most likely in cases treated with neoadjuvant chemotherapy)

Definition of regional lymph nodes- Pathological (pN)

<b>pN category</b>	<b>pN Criteria</b>
<b>Pnx</b>	Regional lymph nodes cannot be assessed (e.g., not removed for pathological study or previously removed)
<b>pN0</b>	No regional lymph node metastasis identified or ITC only
<b>pN0 (i+)</b>	ITC only ( malignant cell clusters no larger than 0.2mm) in regional lymph node (s)
<b>pN0 (mo1+)</b>	Positive molecular findings by reverse transcriptase polymerase chain reaction (RT-PCR); no ITCs detected
<b>Pni</b>	Micro metastases; or metastases in 1-3 axillary lymph nodes ; and/or clinically negative internal mammary nodes with micro metastases or macro metastases by sentinel lymph nodes biopsy
<b>pN1mi</b>	Micro metastases (approximately 200 cells, larger than 0.2 mm, but none larger 2.0mm)
<b>pN1a</b>	Metastases in 1-3 axillary lymph nodes, at least one metastasis larger than 2.0mm
<b>pN1b</b>	Metastases in ipsilateral internal mammary sentinel nodes, excluding ITCs
<b>pN1c</b>	pN1a and pN1b combined
<b>pN2</b>	Metastases in 4-9 axillary lymph nodes; or positive ipsilateral internal mammary lymph nodes by imaging in the absence of axillary lymph nodes metastases
<b>pN2a</b>	Metastases in 4-9 axillary lymph nodes (at least one tumour deposit larger than 2.0mm)

<b>pN2b</b>	Metastases in clinically detected internal mammary lymph nodes with or without microscopic confirmation; with pathologically negative axillary nodes
<b>pN3</b>	Metastases in 10 or more axillary lymph nodes; or in infraclavicular ( Level III axillary) lymph nodes; Or positive ipsilateral internal mammary lymph nodes by imaging in the presence of one or more positive Level I,II axillary lymph nodes and micro metastases or micro metastases by sentinel lymph node biopsy in clinically negative ipsilateral internal mammary lymphnodes; Or in ipsilateralsupraclavicular lymph nodes
<b>pN3a</b>	Metastases in 10 or more axillary lymph nodes (at least one tumor deposit larger than 2.0 mm); or metastases to the infraclavicular (Level III axillary lymph nodes)
<b>pN3b</b>	pN1a and pN2a in the presence of cN2b (positive internal mammary nodes by imaging); or pN2a in the presence of pN1b
<b>pN3c</b>	Metastases in ipsilateral supraclavicular lymph nodes

(sn) and (f) suffixes should be added to the N category to denote confirmation of metastasis by sentinel node biopsy or fine needle aspiration/core needle biopsy respectively with NO further resection of nodes

### Definition of distant metastasis (M)

<b>M</b>	<b>M Criteria</b>
<b>Category</b>	
<b>M0</b>	No clinical or radiographic evidence of distant metastases
<b>cM0(i+)</b>	No clinical or radiographic evidence of distant metastases in the presence of tumor cells or deposits no larger than 0.2mm detected microscopically or by molecular techniques in circulating blood , bone marrow, or other non-regional nodal tissue in a patient without symptoms or signs of metastases
<b>MI</b>	Distant metastases detected by clinical and radiographic means (cM) and/or histologically proven metastases larger than 0.2 mm (pM)

Imaging studies are not required to assign cM0

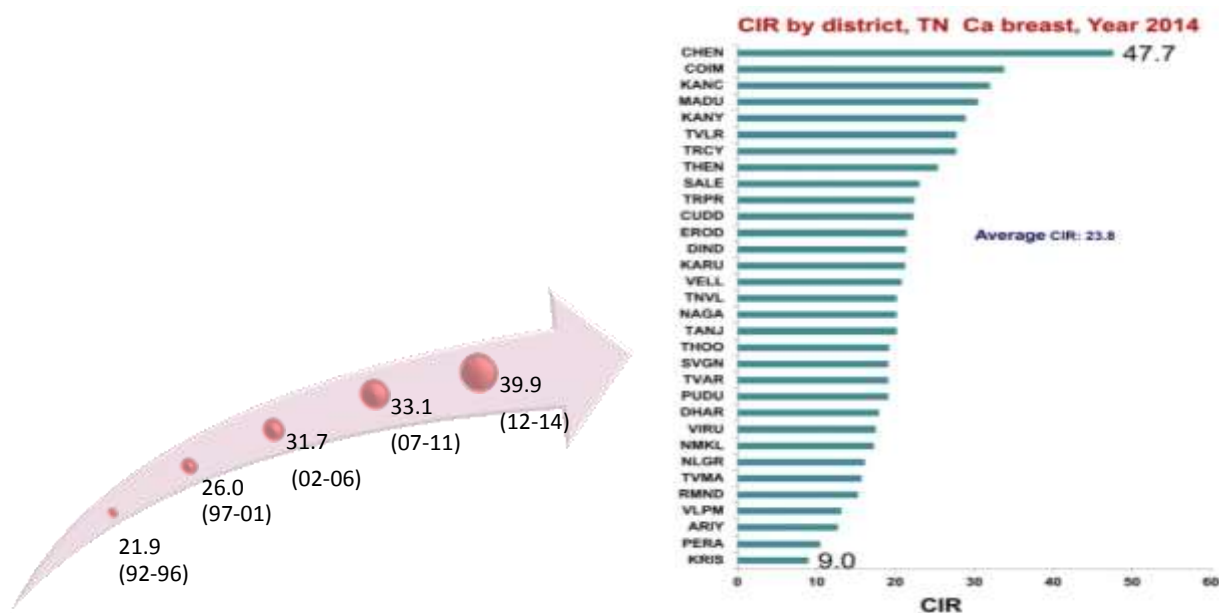


## Stage Grouping

When T is ...	And N is....	And M is ...	Then the stage group is....
Tis	N0	M0	0
T1	N0	M0	IA
T0	N1mi	M0	IB
T1	N1mi	M0	IB
T0	N1	M0	IIA
T1	N1	M0	IIA
T2	N0	M0	IIA
T2	N1	M0	IIB
T3	N0	M0	IIB
T0	N2	M0	IIIA
T1	N2	M0	IIIA
T2	N2	M0	IIIA
T3	N1	M0	IIIA
T3	N2	M0	IIIA
T4	N0	M0	IIIB
T4	N1	M0	IIIB
T4	N2	M0	IIIB
Any T	N3	M0	IIIC
Any T	Any N	M1	IV

## **1.2.b EPIDEMIOLOGY**

Breast cancer is the most common cancer among females worldwide including India. It is the most common cancer in India even when cancers among both sexes are combined. The Crude Incidence Rate (CIR) of breast cancer Worldwide, India (GLOBOCAN: IARC) and Chennai (Madras Metro Politian Tumour Registry-MMTR) for the year 2012 are 47.8, 23.8 and 40.8 respectively. India is experiencing an unprecedented rise in the number of breast cancer cases across all sections of society, as are also other countries. Today, with increasing awareness and screening facilities being available, more number of cases are diagnosed with early breast cancer [1, 2, 3].



**Fig 7: a) Trends of ASR in breast cancers from MMTR, Women**

**b) Crude incidence rates of carcinoma breast**

### **1.3 ROLE OF SURGERY IN BREAST CANCER**

Breast cancer was considered incurable till 17<sup>th</sup> century.

HENRI FRANCOIS LE DRAN HYPOTHESIS (1685-1770) - Breast cancer

spreads in an orderly fashion

William Halsted in 1894 popularised radical mastectomy as the treatment of choice for breast cancer. He considered breast cancer strictly as a loco regional disease.

HALSTEDIAN THEORY- Local and regional nodes are the first echelon of metastatic spread and effective barriers against further spread.

According to him tumor spreads in an orderly pattern and lymph nodes act as barrier to spread. Blood stream is of little significance. The more radical the surgery is, more are the chance of cure. Any recurrence and death are due to inadequacy of surgery.

This led to extended radical mastectomies (Urban- Halsteds + Internal mammary lymph nodes, Dahl Iverson- Halsteds + Internal mammary lymph nodes+ Supra clavicular lymph nodes, Wangenstein- - Halsteds + Internal mammary lymph nodes+ Supra clavicular lymph nodes). But the extended surgeries only added to the morbidity.

## NATIONAL SURGICAL ADJUVANT BREAST PROJECT (NSABP)

Conducted many randomised clinical trials funded by National cancer institute on adjuvant therapy and chemoprevention in breast cancer

NSABP B 04 - scope of reducing the extent of surgery	
Radical Mastectomy (RM) vs Modified Radical Mastectomy (MRM)+ Loco regional Radiation (LRRT)	MRM equivalent to RM in Disease Free Survival (DFS) and Overall Survival (OS)
NSABP B 06 - scope of Breast conservation surgery (BCS) in patients with tumor < 4 cm	
MRM vs BCS + Axillary lymph node dissection (ALND) + RT vs BCS +ALND	No difference in DFS and OS. Ipsilateral Breast Tumor Recurrence was less in BCS + RT arm compared to BCS alone arm
NSABP B 32 – scope of less invasive method of staging the axilla with less morbidity in clinically node negative breast cancer.	
Sentinel node resection (SNR) alone vs SNR + Axillary dissection (AD)	No difference in OS and Loco regional recurrence (LRR)

Randomised multicentre trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer The ALMANAC trial – Sentinel Lymph Node Biopsy (SLNB) is associated with reduced arm morbidity and better Quality Of Life than standard AD and should be the treatment of choice for patients with early stage breast cancer with clinically negative nodes

ACSOG Z011- American College of Surgeons Oncology Group (BCS + Whole Breast Irradiation WBI) Among patients with limited metastasis to SLN treated with breast conservation and systemic therapy, use of SNR alone compared with AD did not result in inferior survival.

ACSOG Guidelines for Management of Sentinel Lymph Node.

BIOPSY RESULTS	GUIDELINES
Negative sentinel node	No further axillary treatment, AD may be omitted
Positive lymph node at presentation (proven by FNAC/core needle biopsy)	AD should be performed
1 or 2 positive Nodes	AD may be omitted if – 1.primary tumour < 5cm 2.clinically negative axilla
3 or more nodes	WBI and likely systemic therapy AD should be performed

ACSOG GUIDELINES are not applicable for patients undergoing mastectomy, receiving neoadjuvant chemotherapy and receiving partial breast radiation or radiation therapy in prone position.

## **1.4 ROLE OF CHEMOTHERAPY (CT) IN BREAST CANCER**

### **FISHER HYPOTHESIS**

Breast cancer is a systemic disease. Tumor cells are likely to have disseminated throughout the body by the time of diagnosis, a condition requiring treatment of the entire patient and treating just the source organ is unlikely to improve survival.

Hematogenous dissemination is as important as lymphatic dissemination. Adjuvant treatment—chemotherapy, endocrine therapy, and targeted therapy—is a mainstay of clinical practice and has led to a substantial decline in breast cancer mortality in women with operable disease

HISTORY – NSABP trials
B-01(Thiotepa vs placebo) Short course perioperative Thiotepa showed advantage in premenopausal women with more than 4 positive nodes.
B-05- L PAM (L phenylalanine mustard, Melphalan) given orally for 2 years for node positive women with breast cancer showed DFS and OS advantage
B-10 – The use of a combination of chemotherapy and immunotherapy [L-PAM + 5 Fluoro Uracil +/- <i>Cryptosporidium parvum</i> and hydrocortisone] was not found to have any advantage over chemotherapy alone.
B-11 The addition of Adriamycin to L-PAM and 5FU was found to be associated with better OS in node positive and Estrogen Receptor (ER) negative tumors
B-13 Sequential Methotrexate and 5 Fluro Uracil for women with node negative ER negative tumors showed OS benefit.

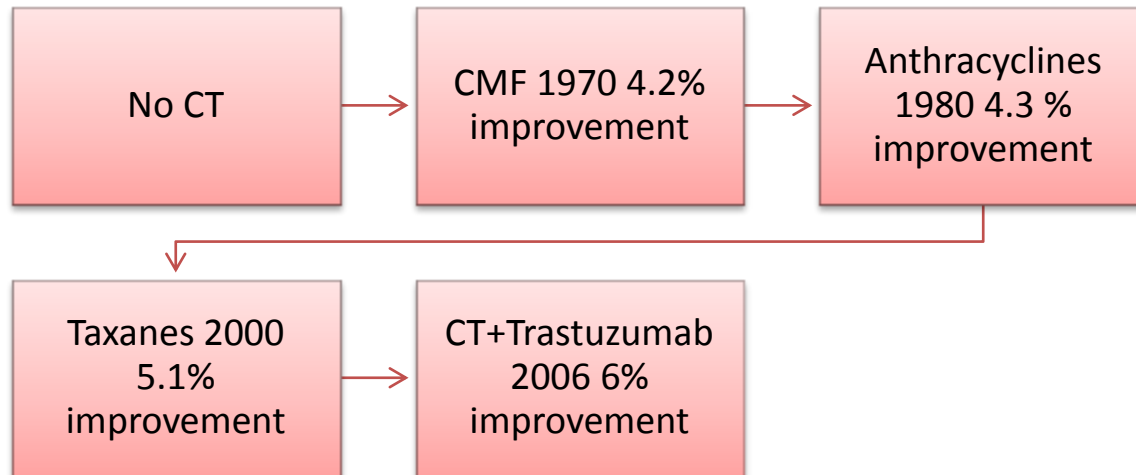


Cyclophosphamide, Methotrexate and 5-Fluorouracil (CMF)		
Milan et al	CMF x 1 year versus observation	improvement in DFS and OS- 47% compared with 22% in observation arm
	12 months of therapy offered no advantage over 6 months but toxicity increased.	
EBCTCG	Poly-chemotherapy versus none	improvement in absolute risks of recurrence and breast cancer mortality
	Benefits are evident in both node-negative and node-positive populations, regardless of age.	
Anthracyclines		
Intergroup-0102	CAF vs CMF (high-risk, node-negative population)	No difference in DFS, but a slight improvement in OS.
NSABP B-15	CMF 6 months vs AC x 4	similar benefits in DFS, distant DFS, and OS
NSABP B-23	2 x 2 classic CMF X 6 versus AC x 4 (Node negative)	Similar
Gains appeared to be maintained in both younger and older women independent of hormone receptor status		
Taxanes		
CALGB 9344	Addition of paclitaxel to four cycles of AC (node positive)	Improvement in DFS and OS
	Preferential benefit for ER-negative over ER-positive tumors	
NSABP B-28	Paclitaxel x 4 after AC X 4 (node-positive)	improvements in DFS but not OS at 5 years
Meta-analysis	Addition of a taxane to anthracycline-based adjuvant regimen	risk of recurrence (17% relative reduction) and OS (15% relative improvement)
Taxanes concurrent vs sequential		
BCIRG 005	TAC vs AC-T	AC-T was not more effective than TAC, different toxicity
NSABP B 30	AC-T, AT, TAC	Sequential better than concurrent and AT non inferior to TAC

Early Breast Cancer Trialists' Collaborative Group (EBCTCG), CAF

(cyclophosphamide, doxorubicin, fluorouracil), AC (doxorubicin  
cyclophosphamide)

Adjuvant chemotherapy should be started 2 to 6 weeks of surgery, significant decrease in the efficacy of CT is observed when administered more than 12 weeks from surgery.



### **DOSE DENSE CHEMOTHERAPY - NORTON AND SIMON HYPOTHESIS**

Tumor follows Gompertzian growth function- Growth rate of populations are exponential at early stages of development and slower at later stages, smaller tumors grow faster than larger ones. Rate of cell killing by drugs is usually proportional to tumor growth rate. Tumors given less time to regrow between treatments are more likely to be destroyed. Therefore High density dosing ie shortening the interval between chemotherapy treatments from 3 weeks to 2 weeks will improve survival. CALGB 9741- Dose density improved DFS and OS, no difference was seen between sequential or concurrent schedule.

## INDICATIONS FOR CHEMOTHERAPY

- 1) Tumor size > 1 cm
- 2) Node positive breast cancer
- 3) Node negative with high risk features (high grade/size of tumor >2 cm, triple negative, Her 2 positive)

### Systemic treatment for early breast cancer subtypes

Subtype	Recommended therapy
Luminal A like	Endocrine (ET) therapy alone in the majority of cases Consider Chemotherapy (CT) if High tumor burden ( 4 or more positive Lymph nodes, T3 or higher) Grade III
Luminal B like (Her 2 Negative)	ET + CT for the majority of cases
Luminal B like (Her 2 Positive)	CT + anti Her 2 + ET for all the patients
Her 2 Positive (non-luminal)	CT + anti Her 2
Triple negative (ductal)	CT

## GENOMICS TO SELECT PATIENTS FOR CT

OncotypeDx / Recurrence Score assay for patients with ER + Lymph node negative disease. Analyses 16 cancer and 5 reference genes.

Category	RS 0-100
Low risk	RS < 18
Intermediate risk	RS $\geq$ 18 to $\leq$ 31
High risk	RS $\geq$ 31

Mammaprint, Adjuvant online, NPI- Nottingham Prognostic Index, Predict score

## **1.5 ROLE OF HORMONAL THERAPY- SCHINZINGER HYPOTHESIS**

Based on postmenopausal breast atrophy and more virulent tumor growth in premenopausal women Schinzinger proposed that Oophorectomy might be of benefit in breast cancer.

Thomas Beatson showed that with surgical oophorectomy there is significant tumor regression, better sense of well-being and regression of cutaneous metastasis.

Endocrine therapy of breast cancer represents the first molecularly targeted therapy for cancer. It can be used in Adjuvant, neoadjuvant, metastatic as well as prophylactic settings.

Drugs/methods for estrogen suppression

SERM	Tamoxifen, Toremifene
Androgens	Fluoxymesterone
Progestins	Megestrol acetate, Medroxyprogesterone acetate
Aromatase inhibitors	Letrozole, Anastrozole, Exemestane
Steroid Antiestrogens	Fulvestrant
LHRH agonists	Leuprolide, Goserelin
Gland ablation	Ovary, Pituitary, Adrenals

All endocrine therapies target Estrogen Receptor (ER) protein, which is present in 70% to 80% of female breast cancers. The progesterone receptor (PR) has not been utilized as a treatment target itself, but its presence indicates a functioning ER pathway because it is an estrogen-induced gene, and, thereby, a tumor that is more likely to be inhibited by ER-targeted therapies.

**ESTROGEN RECEPTOR:** When ER $\alpha$  is bound by estrogen, it activates transcription of specific genes and inhibits transcription of others. Some of these induced genes encode proteins important for tumor cell growth and survival and, consequently, therapies designed to block this pathway have therapeutic benefit.

**SERM-** Selective activation and inactivation of co-repressors and co-activators. Tamoxifen has been the standard for adjuvant endocrine therapy for breast cancer.

- EBCTCG overview Tamoxifen administered for 5 years resulted in a 41% reduction in the annual rate of breast cancer recurrence and a 34% reduction in the annual death rate for women with ER positive breast cancer. These benefits are independent of age, menopausal status, use of adjuvant chemotherapy and are durable, contributing to improved survival.
- The Adjuvant Tamoxifen: Longer Against Shorter trial (ATLAS) compared 10 years versus 5 years of adjuvant tamoxifen, and found an improvement in OS and DFS with the longer duration of tamoxifen treatment.

## AROMATASE INHIBITORS (AIs):

AIs inhibit the aromatase enzyme that converts androgens into estrogens resulting in estrogen depletion. In postmenopausal patients, where only non-ovarian, baseline levels of aromatase activity are present, AIs lower estrogen production to nearly undetectable levels. AIs are not appropriate for premenopausal patients, as residual ovarian function can lead to enhanced production of aromatase and thus overcome the effects of AIs.

Type I Enzyme inactivators (steroidal) exemestane

Type II competitive antagonists (non-steroidal) anastrozole/letrozole

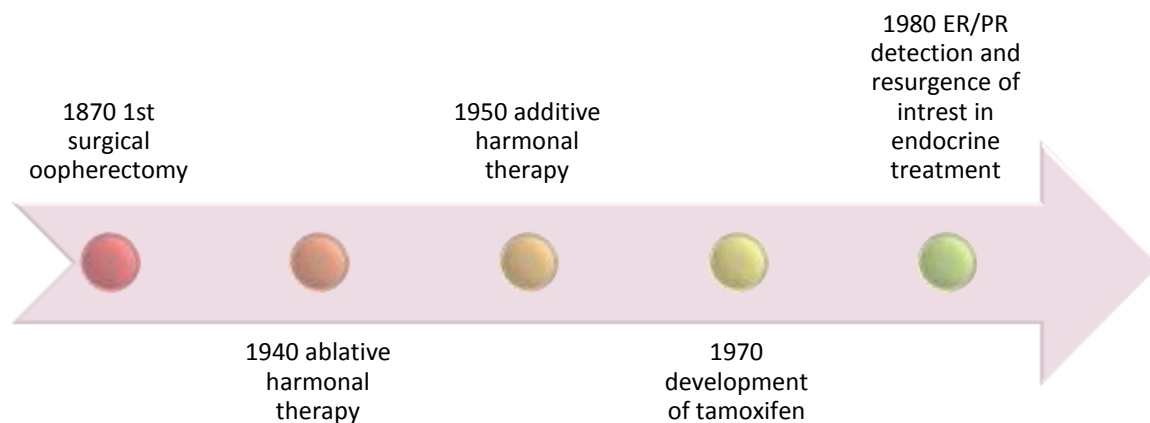
- AI treatment achieved modest improvements in DFS as a result of a lower risk of both distant metastasis as well as of in-breast recurrences and contralateral tumors.
- The recently updated ASCO guidelines on adjuvant endocrine therapy recommend that postmenopausal women to be considered for AI at some point in their treatment program as either initial therapy or as sequential therapy after several years of tamoxifen.

Differences in side effect profiles between tamoxifen and AI therapy may influence treatment selection. Tamoxifen is associated with rare risks of thromboembolism and uterine cancer. AI treatment is associated with accelerated osteoporosis and an arthralgia syndrome. Both treatments are associated with

menopausal symptoms, such as hot flashes, night sweats, and genitourinary symptoms, including sexual dysfunction.

Because AI therapy is only effective in postmenopausal women, tamoxifen remains the treatment of choice in women who are pre- or perimenopausal, or in whom there is question of residual ovarian function. In particular, women with chemotherapy-induced amenorrhea may have recovery of ovarian function and are not suitable candidates for AI treatment.

## **HISTORY OF HORMONAL THERAPY**



1977 Tamoxifen- Competitive binding to estrogen receptors resulting in reduction of transcription of estrogen regulated genes. Cells blocked in G1 phase- cytostatic drug.

1995 Anastrozole, 1997 Toremifene, 1997 Letrozole, 1999 Exemestane

2002 Fulvestrant- steroidal anti estrogen with higher affinity for ER than tamoxifen

2012 Everolimus Dual targeting- Mtor inhibitor avoid resistance to endocrine therapy

2015 Palbociclib Cyclin dependent kinase CDK 4/6 inhibition – put break on cell growth and pushes cells towards death.

Ovarian ablation- permanent cessation of menstruation surgical/radiation

Radiation induced oophorectomy- non-invasive cheap procedure, low dose-carries little additional morbidity, takes time for effect 2-3 months, best for patients with slow progression of disease (improved survival)

Tamoxifen and chemotherapy

Advantage, elimination of both chemoresistant and tamoxifen resistant cell populations, inhibit p-glycoprotein which enhances the sensitivity to doxorubicin, apoptosis inhibitor bcl2 is down regulated

Dis advantage- cytostatic nature of tamoxifen may interfere with chemotherapy by locking cells in chemoresistent phases of cell cycle, antagonises calmodulin and is an  $Ca^{+2}$  channel antagonist that could alter drug uptake



## **1.6 ROLE OF RADIOTHERAPY IN BREAST CANCER**

### **Post Mastectomy Radiotherapy (PMRT)**

Risk of loco regional failure at 10 years post BCS and Systemic therapy is 6-39 %.

Risk of loco regional failure at 10 years post mastectomy and systemic therapy for node negative, 1-3 node positive, 4 or more nodes positive, tumor size > 5 cm and close/positive margins are 5-10%,10-15%,20-30%, > 20% and 45 % respectively.

(ECOG, NSABP 2002), According to EBCTCG meta-analysis isolated local recurrence without radiation is 30.6 % and with radiation is 10.3 % (Absolute difference in risk of isolated local recurrence is 20%) and occurs mostly with in first 5 years. And 15 years breast cancer mortality with and without radiation are 44% and 48.1% respectively. (Absolute difference in risk of death from breast cancer is 4 %), it occurs mostly after 5 years. There is little difference in breast cancer mortality during first 5 years. Preventing 4 recurrences prevents 1 breast cancer death.

Therefore, for patients treated with mastectomy, based on the available evidence from several randomized clinical trials (RCT), chest wall and regional radiation therapy has been shown to significantly reduce local regional recurrence (LRR) and to significantly prolong OS for patients with positive axillary nodes.

## Indications for post mastectomy radiotherapy

- i) Tumor size > 5 cm
- ii) Skin/chest wall infiltration
- iii) Node positive disease
- iv) Extra capsular invasion/perinodal spread

The recent EBCTCG meta-analysis published in 2014 looked at the role of PMRT in women with 1-3 lymph nodes involved. PMRT reduced loco regional recurrence, overall recurrence and breast cancer mortality even when systemic therapy was given. The 10 year LRR was 21% without RT and 4.3% with RT. The 20-year breast cancer mortality was 49.4% with no RT vs. 41.5% with RT [14].

Results from the NCIC MA.20 trial demonstrated that in lumpectomy patients with 1–3 positive nodes (some high-risk node-negative patients were also included), the addition of regional nodal radiation to breast significantly reduced regional nodal recurrence and significantly prolonged disease-free survival (DFS) and distant disease-free survival (DDFS). Also, a non-significant trend in prolonging OS was shown with the addition of regional nodal radiation [15].

Collating data together, the recent consensus guidelines from the National Comprehensive Cancer Institute (NCCN) states that patients with one to three involved lymph nodes who undergo mastectomy should be “strongly considered” for radiation therapy to chest wall, infraclavicular region, supraclavicular region, internal mammary nodes and any part of axillary bed at risk. (Category 2A Based upon lower level evidence there is uniform consensus that the intervention is appropriate) [16, 17].

#### ASCO GUIDELINES [46, 47]

Patient subset	2014	2016
Preoperative systemic therapy	Insufficient evidence whether all patients to be considered for PMRT	In patients with negative/complete pathological response – insufficient evidence to omit radiation
Patients with T < 5 cm and one to three positive axillary lymph nodes	Insufficient evidence	Strongly recommended (Subset with higher risk than benefit with PMRT Age >45yrs/T1+ one small node+ No LVI/Good response to Neo adjuvant chemotherapy)
Regional nodal irradiation in one to three positive axillary lymph nodes		
Supraclavicular-axillary apical nodal irradiation	Insufficient evidence	Generally administered when PMRT is used. (Insufficient evidence to define subgroups with limited benefit)
Internal mammary nodal irradiation	Insufficient evidence	Generally administered when PMRT is used. (Insufficient evidence to define subgroups with limited benefit)
Axillary nodal irradiation	Full axillary irradiation not be given to patients with complete or Level I-II axillary dissection	Recommended for T1-2 with one/two nodes positive on sentinel lymph node biopsy at the time of mastectomy and axillary lymph node dissection not done

On the basis of the above results, chest wall and regional nodal radiation are commonly prescribed for mastectomy patients with positive axillary nodes. More number of patients are being considered for radiation today. This necessitates the need for studying the incidence of morbidity to OAR's as these patients tend to live longer.

### **1.7.a RADIOBIOLOGY of LUNG**

Lung is an intermediate to late responding tissue with  $\alpha/\beta$  ratio of 3Gy. Acute toxicity can occur 2 to 3 months after treatment and presents as pneumonitis. Late toxicity can occur over months to several years later and presents as fibrosis. Most common symptoms are dry cough, dyspnoea and low grade fever. Progressive pulmonary fibrosis may develop in symptomatic patients as well as previously asymptomatic patients. Severity of pulmonary toxicity increases with increasing time and usually is irreversible. Factors determining the severity are Volume irradiated, Dose and fraction size. The target cells are pulmonary endothelial cells and type II pneumocytes which produce surfactant. The Functional sub unit of lung (Pulmonary lobule- terminal bronchiole +respiratory parenchyma) are arranged in parallel. Hence, lung is dose limiting only if large volumes are irradiated or remaining lung is not capable of providing adequate function.

Acute and chronic pneumonitis	TD 5/5Gy	TD50/5 Gy
Field size- Whole lung	17.5	24.5
Field size- 1/3 <sup>rd</sup> lung	45	65

### QUANTEC (Qualitative Analysis of Normal Tissue Effects in the Clinic)

Recommended dose volume limits.

There is no specific threshold for pneumonitis and its risk increases with dose. No optimal dose volume parameter found. For Non-small cell lung carcinoma V20 < 30 – 35 % (Volume of lung receiving  $\geq$  20 Gy should be less than 30 – 35 % of the ipsilateral lung volume) and Mean lung dose < 20 to 23 Gy reduces the risk to < 20%.

#### **1.7.b RADIATION PNEUMONITIS**

The role of post mastectomy radiation (PMRT) in breast cancer patients with 4 and more nodes is well established. Radiation treatment is an important component in the multimodality treatment of breast cancer. The addition of loco regional radiation after surgery and chemotherapy has improved loco regional control by eliminating the occult local disease which is believed to be the focus for breast cancer related events like recurrence and systemic metastasis even though chemotherapy was administered after mastectomy. Thus the addition of radiation has improved loco regional control which has translated into OS.

Recently evidences have accumulated in support of PMRT even among patients with 1-3 lymph nodes involved. With increasing number of early breast cancer patients diagnosed with 1 – 3 nodes, more number of patients are being considered for post mastectomy loco regional radiation (LRRT). The appropriate radiation volumes to be encompassed are uncertain. The addition of lymphatic radiation increases the risk of acute and late side effects to lung and heart, the organs at risk (OAR).

Today there is an increase in the number of young onset early breast cancers requiring LRRT. The effects of radiation on the lungs, both acute and long term is valuable. Literature mentions that the incidence of symptomatic radiation pneumonitis is less than 1% when only chest wall or breast radiation is given and between 4 to 11% after LRRT. With the delivery of multimodality treatments in node positive patients and resultant increase in life expectancy, the need to study the effects of radiation on lungs is obvious.

Little is known about the impact of treating the supraclavicular (SCL) fields, but it has generally been believed that these are of less importance in the development of symptomatic pulmonary complications due to the low pulmonary blood flow in this volume. Therefore, even though the lung volume irradiated is increased due to additional radiation to regional node this increased lung dose may not lead to significant pulmonary toxicity and functional compromise [13].

Chemotherapy – Cyclophosphamide, Methotrexate, Taxanes are all associated with pneumonitis. Paclitaxel given concurrent and close in temporal proximity to radiation may cause increased radiation pneumonitis, However sequential paclitaxel and radiation with a gap of 3-4 weeks has very low risk of radiation pneumonitis [48, 49]

Tamoxifen- Effect of concurrent tamoxifen depends on the inherent radio sensitivity of the individual. Tamoxifen induces the synthesis of Circulating transforming growth factor  $\beta$  (TGF  $\beta$ ), a major participant in the process of wound healing and fibrosis, this may speed up the vicious cycle of chemo-taxix and activation of neutrophils, T lymphocytes, monocytes, and fibroblasts initiated by radiotherapy. Tamoxifen stimulates secretion of TGF  $\beta$  by the fibroblasts but plasma level of TGF  $\beta$  levels may not represent the insitu TGF  $\beta$  [50] or radiation induced cd8 lymphocyte apoptosis RILA. Tamoxifen Concurrent with radiation increased risk of fibrosis (lung, subcutaneous) aromatase inhibitors and taxane based chemotherapy no such effect is seen. But, no data is available on long term toxicity. Letrozole- low has RILA [49, 50]

Pneumonitis in sequentially administered trastuzumab is rarely seen

## ***ASSESSMENT OF RADIATION PNEUMONITIS***

Clinical- Signs and symptoms (RTOG grading)

Radiological- Chest X-ray/ CT Scan

Functional- Pulmonary function tests

Biochemical- plasma TGF- $\beta$  Levels [50]

Genetic- Presence of ATM gene is associated with increased risk  
of development of radiation pneumonitis

Pathological- Biopsy

DVH - Three-dimensional treatment planning provides detailed information about the doses received by the OAR. Various investigators have demonstrated relationship between lung parameters like percentage volume of lung receiving a dose of 20 Gy (V20) [6,7], Dose received by 25% of lung (D25) [7], Mean lung dose (MLD), Central Lung Distance (CLD) and age as factors for causing radiation pneumonitis (RP) [9, 10, 11, 12].

The purpose of my study is to analyse the toxicity to lung following loco regional radiation and the impact of regional nodal irradiation especially supraclavicular radiation and its association with Radiation Pneumonitis. From the 3D planning, the CLD of the tangential field, Apical Lung Distance (ALD) of the supraclavicular field and from the Dose Volume Histogram (DVH) factors like V20, D25, MLD, minimum and maximum doses are generated. Its association with radiation pneumonitis (radiological and symptomatic pneumonitis) will be analysed.



## **1.8 LITERATURE REVIEW**

### **Studies on different radiation techniques, Lung doses with these techniques and estimated risk of Radiation Pneumonitis**

Ibrahim Awad et al, compared average lung dose distribution for 36 breast cancer patients treated with LRRT in two dimensional radiotherapy (2D-RT) and three dimensional conformal (3D-CRT) radiotherapy planning techniques. There was an obvious lesser lung dose with 3D CRT compared to 2D RT planning [18].

Ibrahim Awad et al	2D-RT	3D-CRT
V 20	30±5 %	22.2±5.3 %
Ipsilateral mean lung dose	1614±369 cGy	1217±279 cGy

*Source:* Med. J. Cairo Univ., Vol. 81, No. 1, March: 21-27, 2013

Salah El-Mesidy et al evaluated left lung radiation doses in 30 left breast cancer patients treated with LRRT (Internal mammary nodal IMN regions included) using 3D-CRT and Intensity modulated radiotherapy (IMRT) planning and showed that IMRT planning improved target coverage and decreased irradiation of the OAR at the expense of increased target heterogeneity and more radiation doses to contralateral breast compared with 3D-CRT [19]

Salah El-Mesidy et al	3D-CRT (mean ± S.D) Partially wide tangent fields (PWTfS)	IMRT (mean ± S.D) 7 coplanar equi-angular beams
V 20	28.67 ± 5.53%	17.21 ± 2.46%
Dmean	1291.65 ± 325.55 cGy	1436.00 ± 193.29 cGy
NTCP	3.710 ± 2.89%	0.96 ± 0.39%

*Source:* Pan Arab Journal of Oncology, vol 4; issue 4, December 2011

Pierce et al compared the lung doses of 20 post mastectomy LRRT patients using 7 different planning techniques and estimated the risk of RP. Using techniques that include IMNs resulted in a 10% increase in the lung V20 compared to standard tangents. Their analysis supported the use of partially wide tangent fields (PWTFs) as the most appropriate compromise for both target coverage and normal tissue toxicity when treating chest wall including IMN [20, 21].

Pierce et al	V20 (Mean±SD)	NTCP
Standard tangents	23.60±6.58 %	0.37±0.48.738%
Electron	28.75±9.94 %	0.79±1.05%
Cobalt	30±10.95 %	2.29±2.49%
Partially wide tangents	31.85±5.23 %	2.38±4.37%
Mixed 30/70 photon/electron	33.45±13.06 %	4.98±7.03%
Mixed 20/80 photon/electron	33.65±10.41 %	6.01±8.73%

*Source:* IJROBP, Vol 52, No 5, Pg 1220-1230, 2001

### **Studies on incidence of radiation pneumonitis**

Pher ARM Lind et al did a retrospective analysis of patients treated with post mastectomy loco regional radiation (Chestwall + IMR + SCL +Axilla). Patients were treated with electrons or partial tangential photons to a Total Dose (TD) of 46 Gy. The incidence of symptomatic radiation pneumonitis in their study is 24% [13, 32].

Sung ho moon et al did a retrospective study. Patients received a TD of 50.4 Gy to whole breast/ Chest wall using tangents (No IMR). Irradiation of SCL when indicated was done using Single Direct Field with photons. They found

symptomatic pneumonitis in 13.9% of patients in tangential territory and 49.2% scl territory [31].

Hak jae kim et al also did a retrospective study. Patients were treated to a TD of 50.4 Gy, IMN region not irradiated. The incidence of symptomatic pneumonitis and radiological pneumonitis was found to be 1.9 % and 22.6% respectively [11].

Zsuzsanna kahan et al did a prospective study, Patients were treated with conformal therapy and they employed CT chest to study radiological pneumonitis. Regions irradiated were CW/breast + IMN region + Axilla + SCL. 7.5% of patients developed acute symptomatic pneumonitis, 35.5% of patients developed late symptomatic pneumonitis and radiological changes suggestive of radiation pneumonitis were present in 37% patients [8].

Mark et al reported a 2.6% risk of clinical pneumonitis in patients treated primarily with PWTs. Only 0.5% of patients, however, had persistent symptoms. They concluded that although pneumonitis is a risk that should be discussed with patients, its risk alone should not deter clinically warranted treatment of the regional nodes [22].

Mark et al(Tangents mostly PWTF, separate IMN field mostly electrons)	Radiation pneumonitis	Percentage
Tangents only, No chemotherapy	3/255	1%
Tangents only with chemotherapy	3/66	5%
Tangents + separate SC and IMN fields, No chemotherapy	0/13	0%
Tangents + separate SC and IMN fields with chemotherapy	0/49	0%
Tangents + separate SC field, No chemotherapy	3/86	3%
Tangents + separate SC field with chemotherapy	7/149	5%
a. With average height of lung shadow: <2 cm	1/47	2%
b. With average height of lung shadow: 2-3 cm	5/61	8%
c. With average height of lung shadow:>3 cm	1/7	14%
d. With average height of lung shadow: unknown	0/34	0%

*Source: IJROBP volume 48, number 3, supplement, 2000 pg 294-295 (2060)*

Radiation pneumonitis has been associated with increasing volume of irradiated lung and chemotherapy use. In a series from the Joint Centre of Radiotherapy, RP was observed in 0.2% of patients treated with tangent breast fields alone compared to 1.4% in women treated with nodal radiotherapy [23].

The use of chemotherapy increased the incidence of RP to 3.3%, and its effect was further increased to 8.8% with concurrent chemotherapy and radiotherapy (RT). Taxane use may also increase this risk [24, 25, 26, 27, 28, 29].

Therefore, it is seen that the incidence of radiation pneumonitis varies with the technique employed, addition of nodal regions, number of fields used, end points chosen for the study – symptomatic/radiological/steroid requiring pneumonitis (Grade) and their definitions, tools used to assess pneumonitis- clinical

assessment/ Chest radiograph / CT scan / Pulmonary function tests / bio-chemical markers / different scoring systems, type of study- prospective / retrospective and the Lung volume irradiated.

From the above studies it is clear that estimates for RP vary by Radiation technique, which largely reflects differences in the volume of irradiated lung. Following careful RT treatment planning, subjective assessments from DBCCG 82b and 82c did not show an increase in the rates of dyspnoea and cough following RT compared with controls. The risk of asymptomatic pulmonary fibrosis, as measured by serial chest radiographs, was, however, increased [30].

## **II. OBJECTIVES AND METHODOLOGY**

### **2.1 AIM:**

To study the incidence of symptomatic and radiologic pulmonary toxicity in patients undergoing post mastectomy LRRT using three-dimensional conformal planning technique and to study the impact of supraclavicular radiation on the incidence of radiation pneumonitis (clinical and radiological) using DVH data.

### **2.2 OBJECTIVES:**

#### **Primary:**

To assess radiological changes in lung and symptomatic pneumonitis following loco regional radiation and its association to patient and treatment related factors including addition of supraclavicular radiation.

#### **Secondary:**

To identify association between the factors mentioned below as a cause for radiation pneumonitis so as to suggest modifications in the constraints during radiation planning as there is no consensus guidelines regarding the factors responsible for radiation pneumonitis available.

a) Patient factor: Age, Total lung volume-Ipsilateral and bilateral.

b) Treatment factors:

i) Chemotherapy details.

ii) Radiation timing with respect to chemotherapy.

iii) Lung doses – V5, V10, V15, V20, V30, V40 and D25 including the minimum, maximum and Mean Lung Dose (MLD), Central Lung Distance (CLD), Mean Lung Distance (average of lung distances of the tangential field at three levels - superior, middle and inferior), Apical Lung Distance (ALD) of the supraclavicular field. Two plans with and without supraclavicular radiation and compared and analysed for the impact of supraclavicular radiation.

## **2.3 PATIENTS AND METHODS**

**TYPE OF STUDY:** Retrospective study

**STUDY PERIOD:** January 2015 to August 2016

**STUDY POPULATION:**

Stage IIA, IIB, IIIA and IIIB patients who underwent post mastectomy loco regional radiation and completed one year follow up at the Institute.

## **STUDY ELIGIBILITY:**

### **INCLUSION CRITERIA:**

1. Patients who received post mastectomy loco regional radiotherapy
2. Invasive histopathology
3. Margin negative
4. Treated with conformal technique using partially wide tangents
5. Completed treatment as per institute protocol
6. Completed one year follow up

### **EXCLUSION CRITERIA:**

1. Patients with supraclavicular and internal mammary nodes.
2. Margin positive.
3. Bilateral breast carcinoma requiring radiation to both chest wall.
4. Patients who underwent breast conservation surgery.
5. Patients considered for Pre-Operative Radiotherapy.
6. Pre-existing pulmonary disease/Chronic respiratory diseases/Autoimmune disease.
7. Previous history of treatment for malignancy.
8. Patients progressed on treatment and during study period.
9. Patients who have radiological changes with proven/suspected infective etiology



### **2.3.b METHODS**

The Patients who were treated with post mastectomy LRRT using conformal technique to chest wall, SCL and IMN regions upto a total dose of 4680 cGy at 180 cGy daily fractions, 5 days a week over a period of 5 to 6 weeks were included in the study. These patients Age, Height, weight, Body mass Index, comorbid, Addictions, Clinical stage, side of radiation, histopathology, Surgery, chemotherapy, hormonal therapy, radiation therapy details including sequencing of treatment were noted.

All patients on radiation were reviewed weekly during treatment and once every 3 months during first one year of follow-up by radiation oncologist and details noted in patient records. Any symptomatic pneumonitis recorded during and after treatment were noted from these records and graded as per Radiation Therapy Oncology Group RTOG toxicity criteria.

## **RADIOTHERAPY TECHNIQUE USED:**

All patients considered for post mastectomy LRRT were treated with CT based three-dimensional conformal radiation technique. A thermoplastic mould was made with the patient in treatment position on the breast board. Three fiducial markers were placed. The medial, inferior and lateral borders of the chest wall fields were marked and radio opaque markers were placed. Planning CT scans were taken with 5mm slice thickness. As per the RTOG contouring guidelines, the PTV was generated after delineating the clinical target volume (CTV) of the chest wall and the IMN (delineated using the internal mammary vessels as surrogate). The heart and ipsilateral and contralateral lungs were delineated as the OAR. Supraclavicular (SCL) fields were contoured as per RTOG guidelines. The chest wall and internal mammary nodal regions were treated with partially wide tangents. In those patients for whom lower internal mammary nodal regions cannot be included in view of increased lung dose (Mean Lung Dose more than 15Gy) or due to increased Heart dose in left sided breast cancers (V25 more than 10%), the upper internal mammary nodal regions up to fourth intercostal space were included in the treatment planning. The supraclavicular region was treated with anterior oblique photon beam calculated at a depth. If coverage is not adequate a small posterior boost was given. Portal images were taken at start and thereafter weekly.

## **CLINICAL ASSESMENT:**

***RTOG Grading Acute Toxicity Lung criteria*** (During treatment and every FU visit)

Gr I Dry cough / dyspnoea on exertion

Gr II Persisting cough requiring narcotics / dyspnoea with minimal effort

Gr III Severe cough unresponsive to narcotics /dyspnoea at rest / clinical or radiological evidence of acute pneumonitis / intermittent O2 or steroids

Gr IV Severe respiratory insufficiency / continuous O2 or assisted ventilation

Serial chest X rays of all these patients at diagnosis, prior to radiation (when radiation is planned sequentially after completion of chemotherapy) and one year after completion of radiation were reviewed by radiologist and radiological pulmonary toxicity was graded as per modified WHO grading system for radiographic pulmonary toxicity.

## RADIOLOGICAL ASSESSMENT:

*Modified WHO Grading System for Radiographic Pulmonary Toxicity [31].*

Parameter		Score
Area of ipsilateral lung involved (A)	None	0
	< 1 / 3	1
	1 / 3 to 2 / 3	2
	> 2 / 3	3
Degree of shadowing (S)	None	0
	Faint	0.5
	Moderate	1
	Dense	1.5
Distortion of anatomy (D)	None	0
	Volume loss	2
Sum (A+S+D)		

## ***MODIFIED WHO GRADING SYSTEM FOR RADIOGRAPHIC PULMONARY TOXICITY(RPT).***



Typical cases of radiographic pulmonary toxicity.

(A) Area of ipsilateral lung involved  $>2/3$  (score 3),

(B) Dense shadowing (score 1.5),

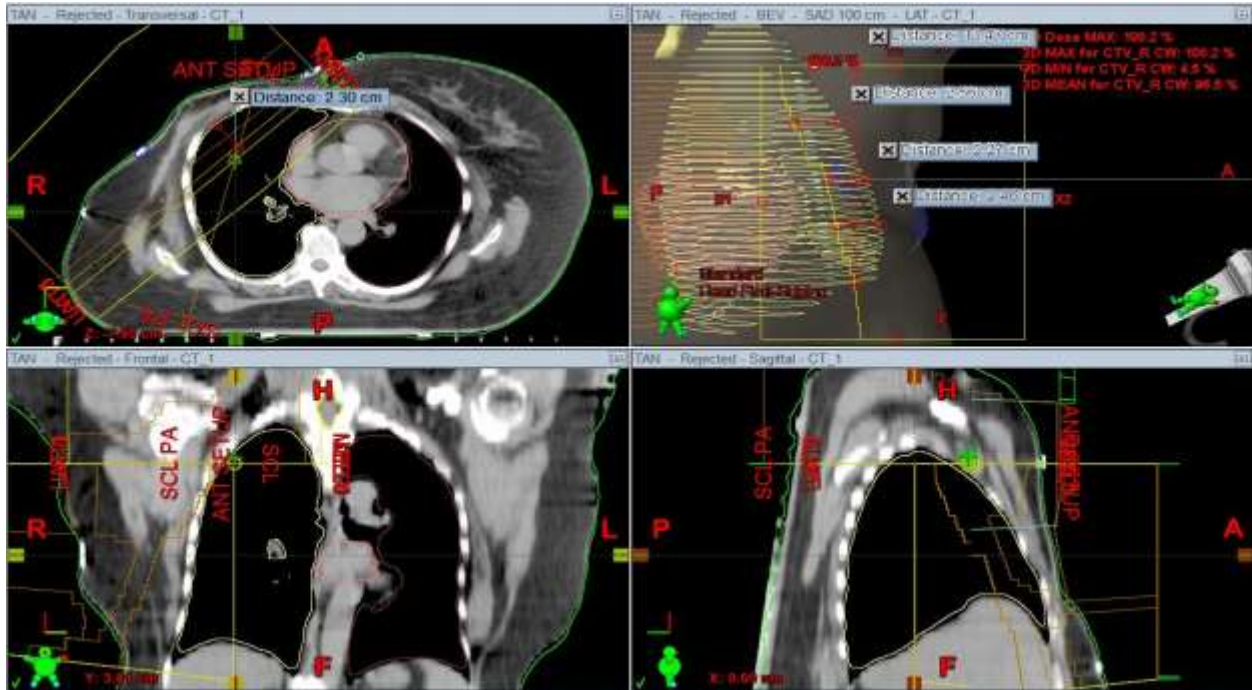
(C) Presence of volume loss (score 2).

## **DVH DATA**

From the treatment plan (Plan 1) the Central Lung Distance (CLD), Mean Lung Distance (average of the superior, middle and inferior tangent) of the tangential field and Apical Lung distance (ALD) of the supraclavicular field will be noted. Lung length (LL) of the tangential field and the DVH provided details regarding lung dose V5, V10, V15, V20, V30, V40 and D25 minimum, maximum and mean lung doses (MLD), ipsilateral and bilateral lung volume are computed and noted.

## LUNG LENGTH (LL)

The maximum vertical length of lung covered in the tangential field



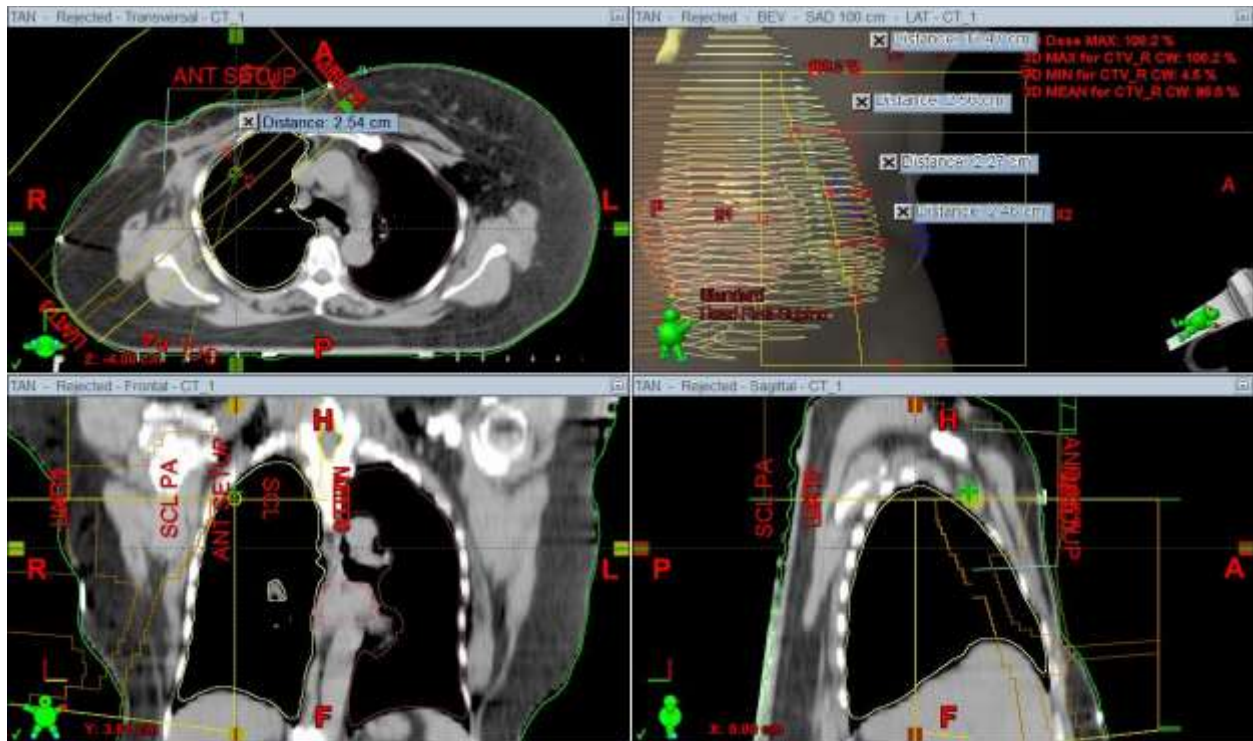
**SUPERIOR LUNG DISTANCE** Distance between a point, at a level half way the midpoint of lung length and upper border of tangential field, of the posterior border of tangential field and the edge of the chest wall

**INFERIOR LUNG DISTANCE-** Distance between a point, at a level half way the midpoint of lung length and lower most extent of the lung covered in the tangential field, of the posterior border of tangential field and the edge of the chest wall

**CENTRAL LUNG DISTANCE-** Distance between the midpoint of the posterior border of tangential field and the edge of the chest wall

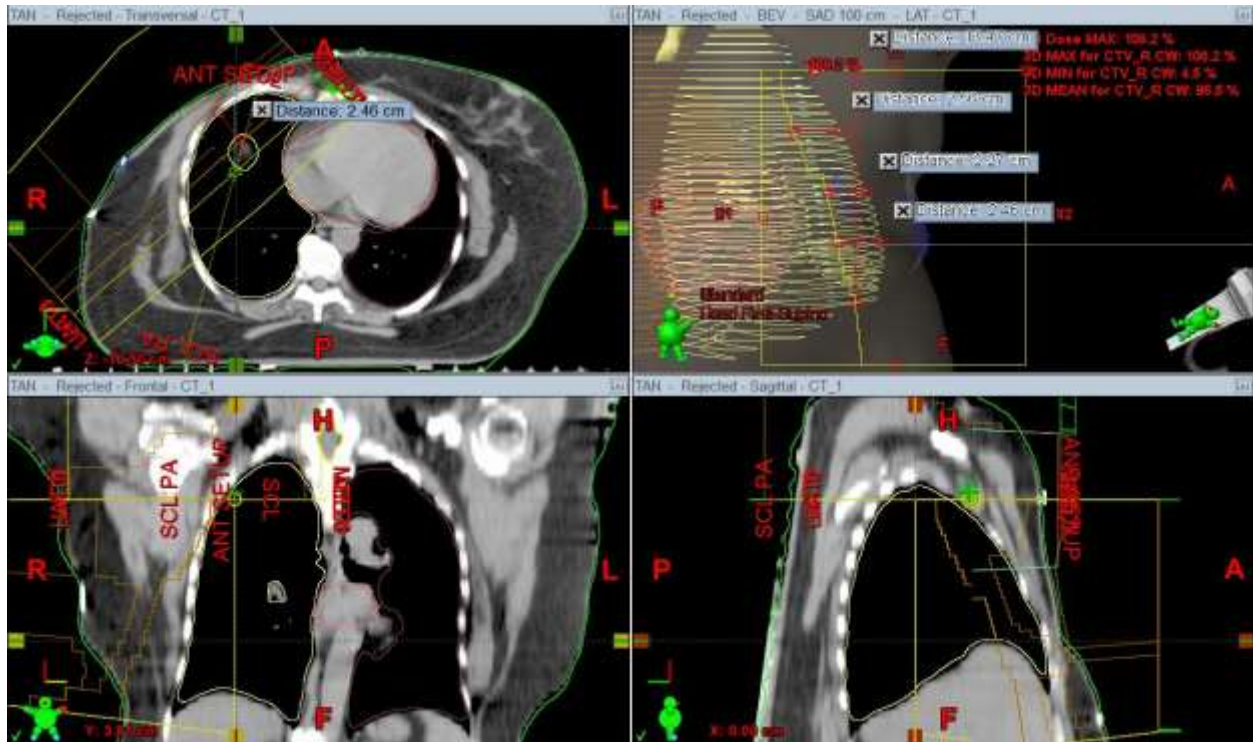
MEAN LUNG DISTANCE - Average of superior, central and inferior lung distance.

### SUPERIOR LUNG DISTANCE

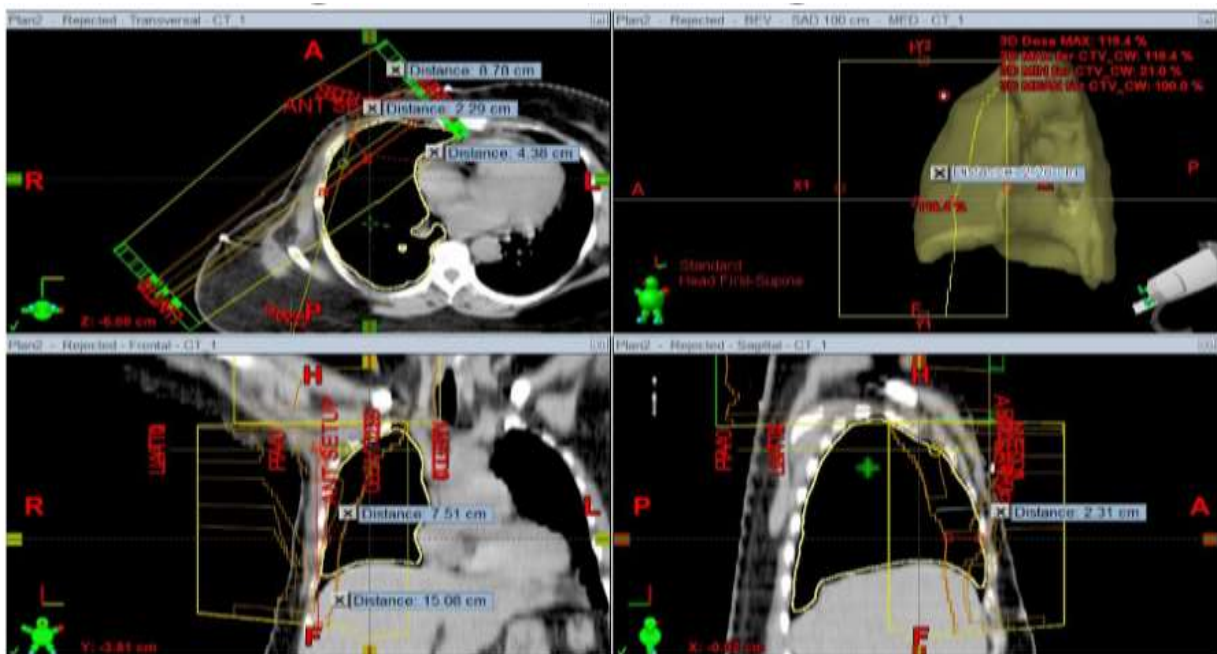




## INFERIOR LUNG DISTANCE



## CENTRAL LUNG DISTANCE (CLD)





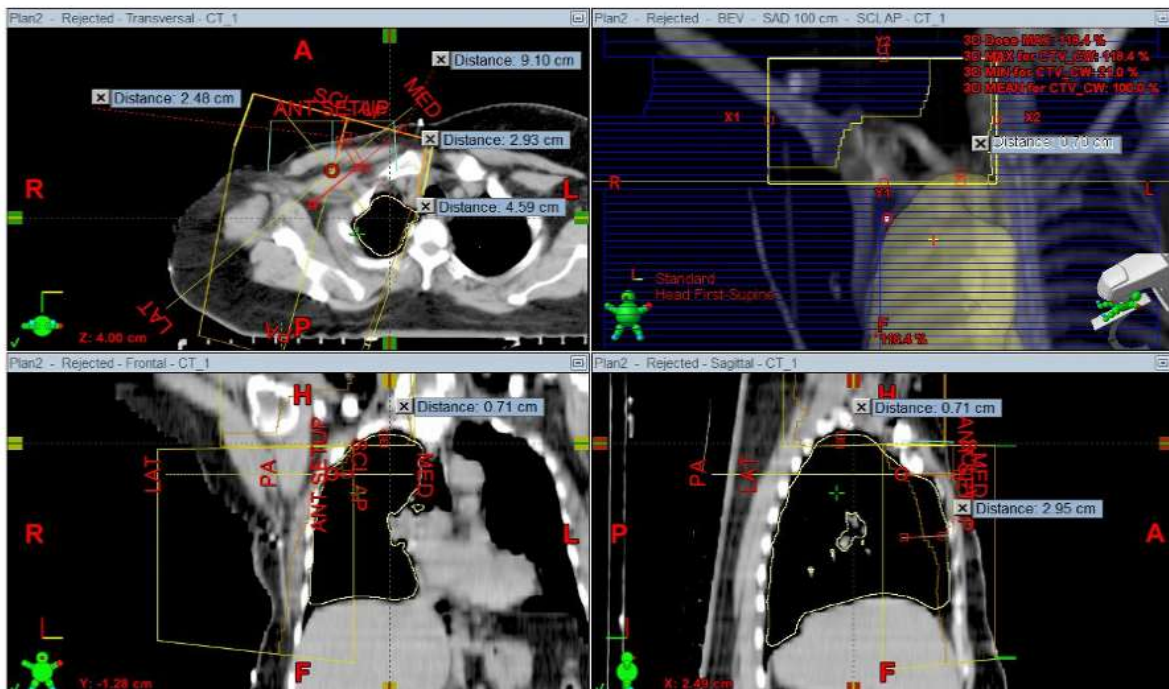
## MAXIMUM LUNG DISTANCE (MLD)

The maximum distance of lung included in the tangential field from beams eye view.



## APICAL LUNG DISTANCE (ALD)

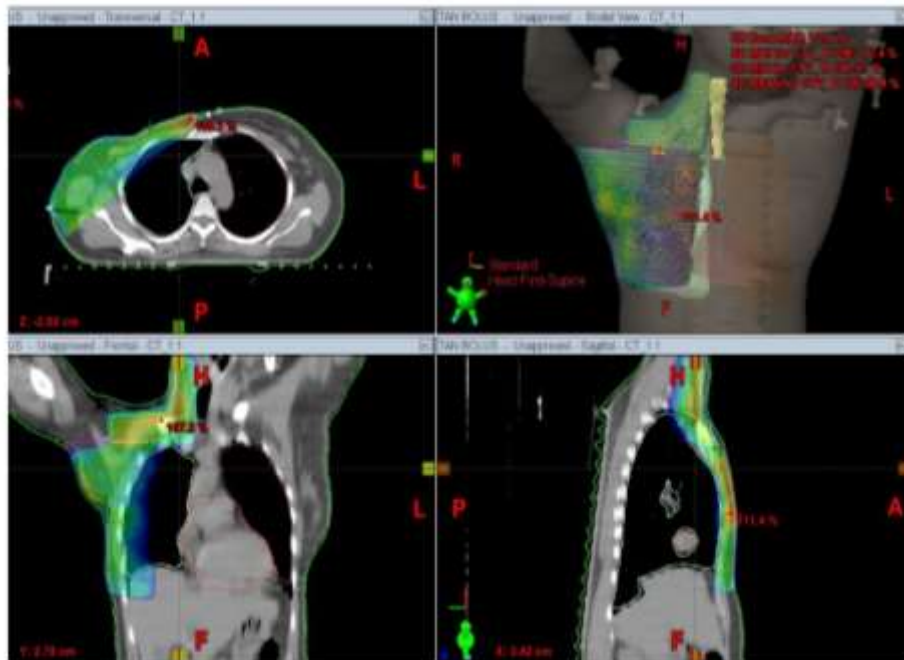
The maximum distance of lung apex involved in the SCL field measured from the field junction.



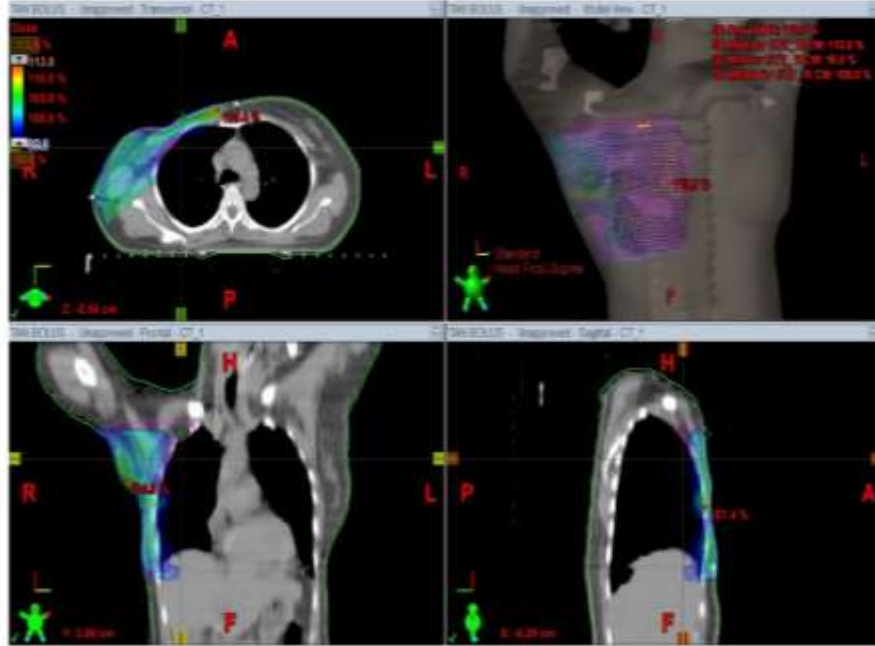
For 30 patients, another plan without supraclavicular field (plan 2) is generated and all the afore said parameter for this plan will also be noted and compared with treatment plan. Binary tables of two plans with and without SCL field (Plan 1- Chest wall + IMN region + SCL) and (Plan 2- Chest wall + IMN regions) are generated and DVH data of both these plans are noted for comparison and analysis.

Binary tables of 2 plans (Plan 1 – Chestwall + IMR + SCL, Plan 2 – Chest wall + IMR) were generated and the different variables CLD, Mean lung distance, Maximum lung distance, Minimum, Maximum and Mean Lung Dose (MLD), Relative and absolute lung volumes V5, V10, V15, V20, V40, D25, Apical Lung Distance (ALD) of the supraclavicular field were analysed using the Paired t test.

### ***DOSE COLOUR WASH WITH SCL FIELD***



## ***DOSE COLOUR WASH WITHOUT SCL FIELD***



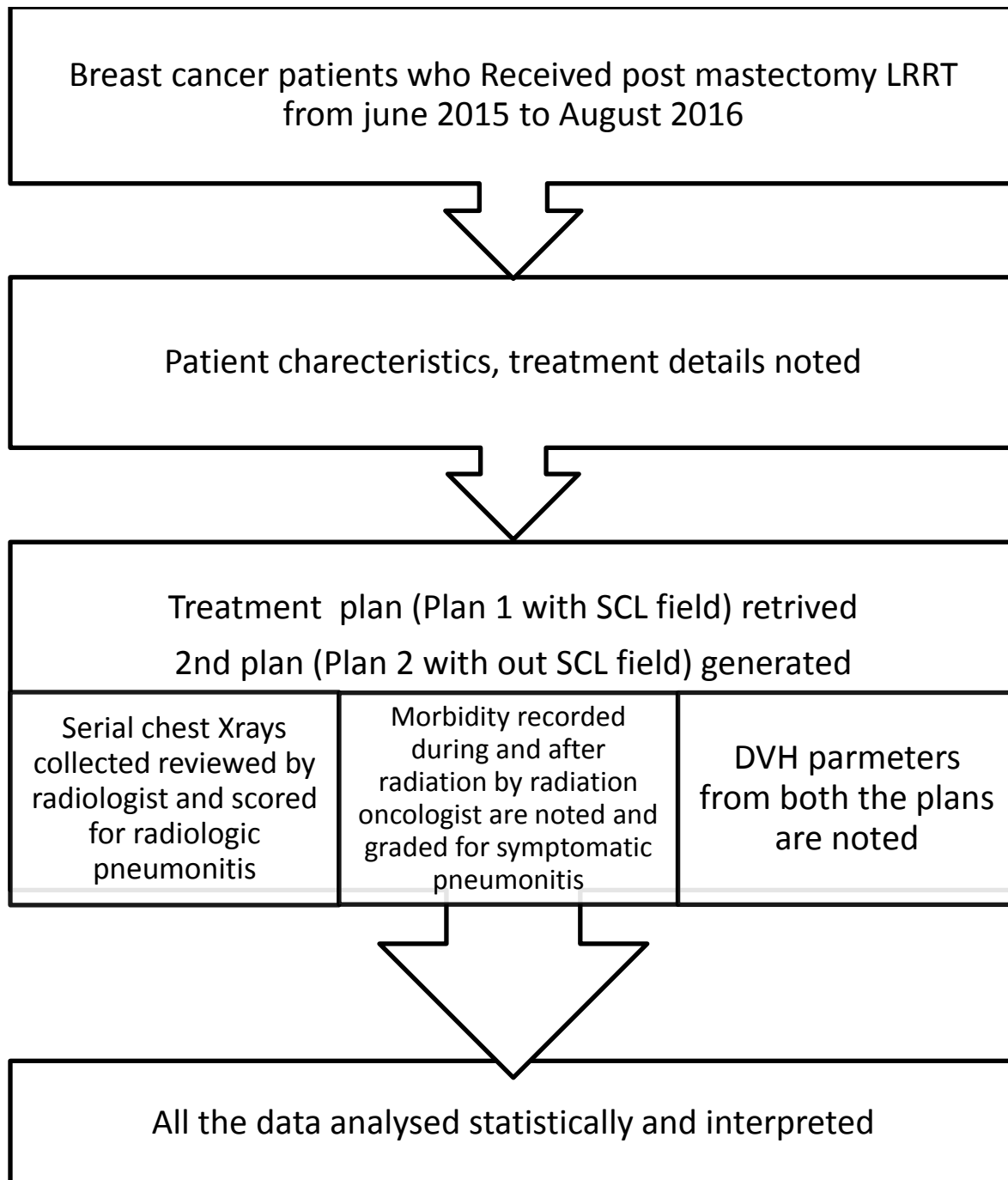
All variables Age, Lung Volume, Chemotherapy, Hormonal therapy, DVH data were analysed for radiological and symptomatic lung morbidity using Non parametric statistical test. All this information was tabulated and statistically analysed and interpreted

## **STATISTICAL METHODS**

Descriptive statistics of variables analysed were given by one way frequency tables and graphs. Association of categorical variables with Radiological radiation pneumonitis was done using chi-squared test. Differences in mean values of variables with absolute measurements with radiological radiation pneumonitis were done using independent student-t test. Receiver Operating Characteristic

curve (ROC) were employed to identify a cut off value with optimal sensitivity and specificity for lung volumes and doses. [31, 51].

## OUTLINE



### **III. RESULTS AND STATISTICAL ANALYSIS**

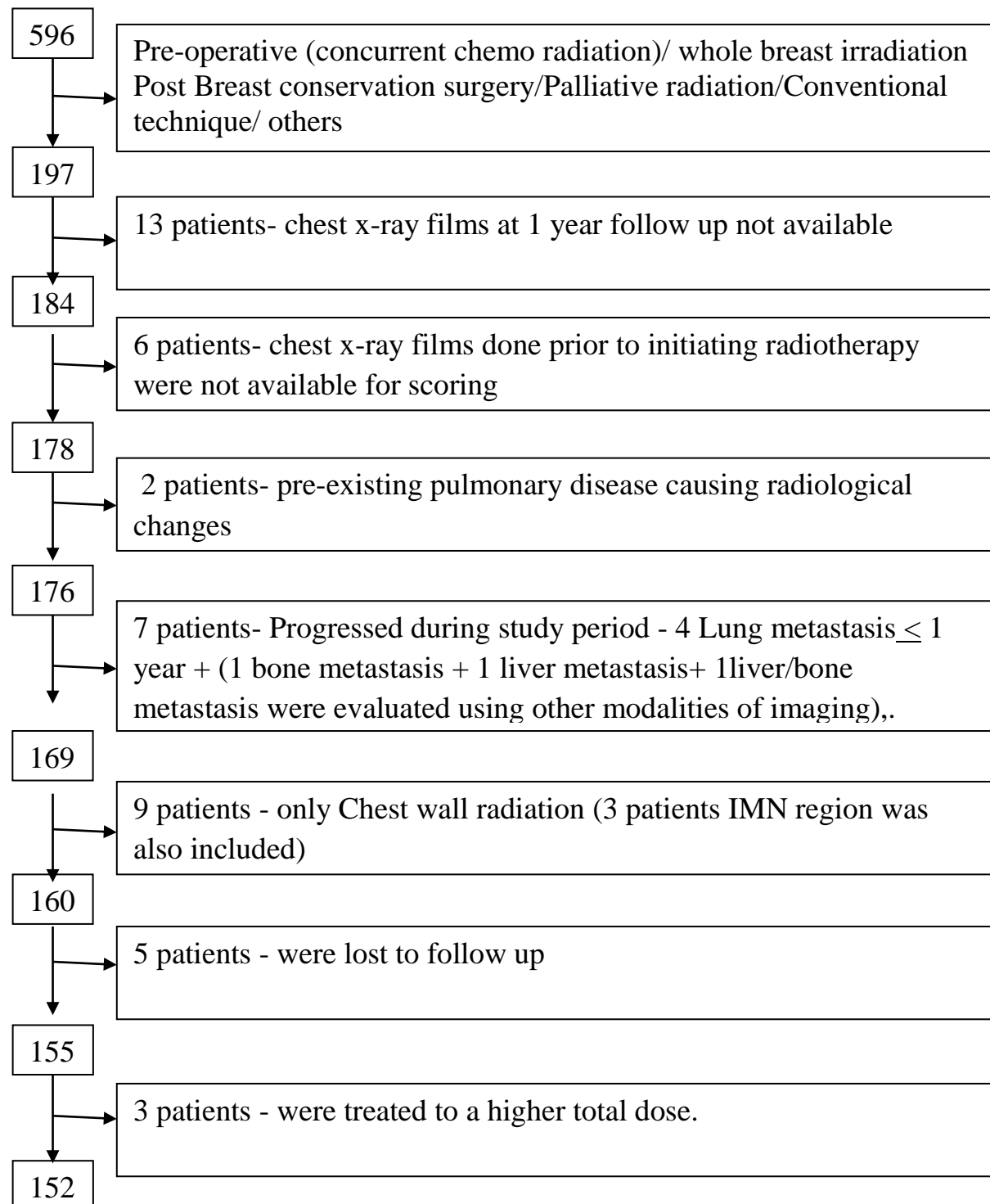
#### **3.a RESULTS:**

2563 patients with complaints of breast lump or suspected/diagnosed breast cancer, reported to our Out Patient Department from January 2015 to August 2016. Of these 1334 patients were diagnosed with breast cancer and were treated at our Institute.

From January 2015 to August 2016, a total of 596 patients received radiation and 197 patients of these were treated with post mastectomy radiotherapy at our institute using conformal technique.

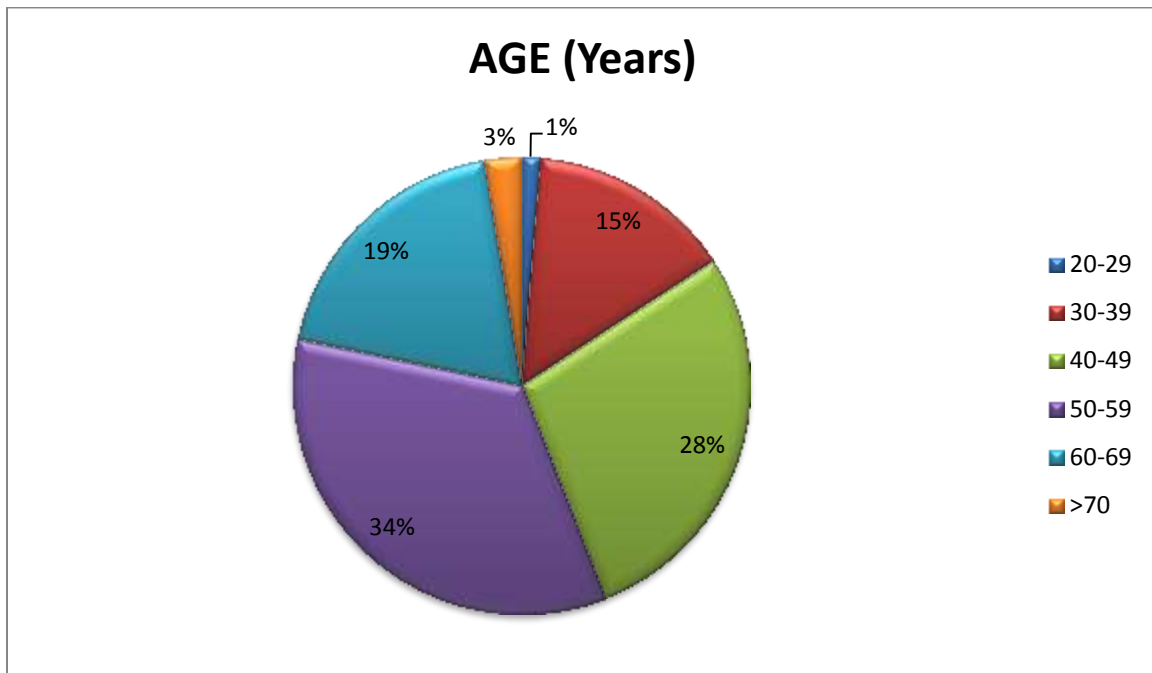
45 patients among these were excluded from the study. 13 patients of them were excluded as chest x ray films at 1 year follow up were not available for assessing radiological pulmonary toxicity. Another 6 patients were excluded as chest xray films done prior to initiating radiotherapy were not available for scoring. 2 patients had pre-existing pulmonary disease causing radiological changes and hence excluded. 7 patients progressed during study period, 3 of them had distant metastasis at sites other than lung (one had bone metastasis, second patient had liver metastasis and the third one had both liver and bone metastasis and were evaluated using other modalities of imaging), and rest of 4 patients had lung metastasis (2 of which were detected on annual investigation and the other 2 had a DFS of less than 1 year). 9 patients for whom only Chest wall radiation was given

(for 3 patients among these 9 IMN region was also included) were also excluded from the study. 5 patients were lost to follow up. Another 3 patients were excluded as they were treated to a higher total dose.



Total 152 patients are included in the study and their characteristics are tabulated below. All patients were women. Follow up duration ranging from 13 to 31 months, mean follow up of 21 months.

Median Age is 50 years. Ranging from 24 to 71 years.



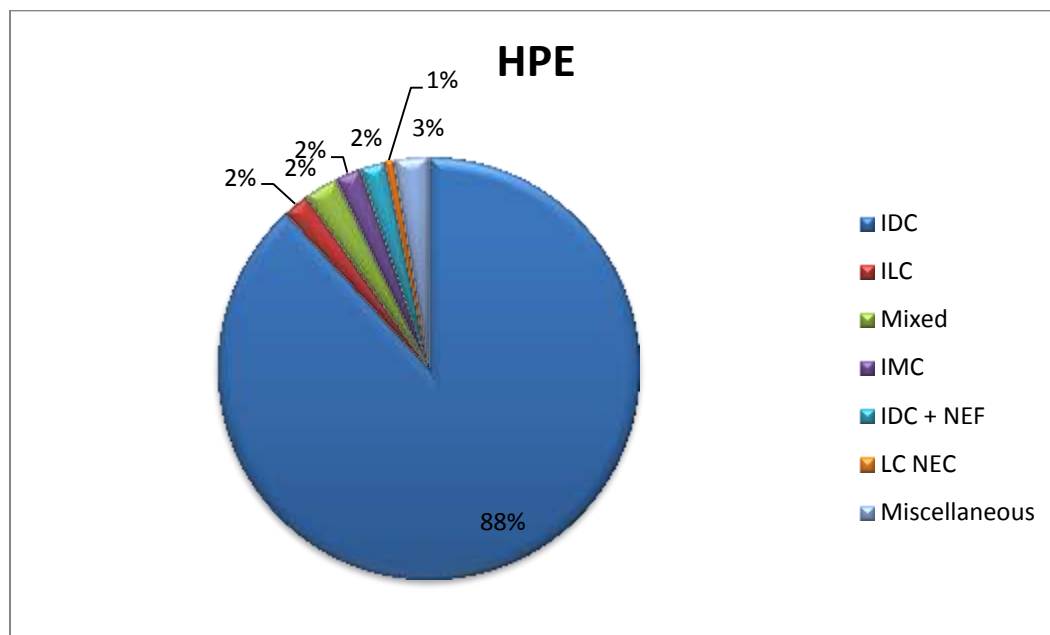
BMI range 16 to 40Kg/m<sup>2</sup>, median 26 kg/m<sup>2</sup>.

20 patients had a habit of chewing tobacco.

31 patients were exposed to passive smoking.

Patient characteristics (Patient factors) n=152

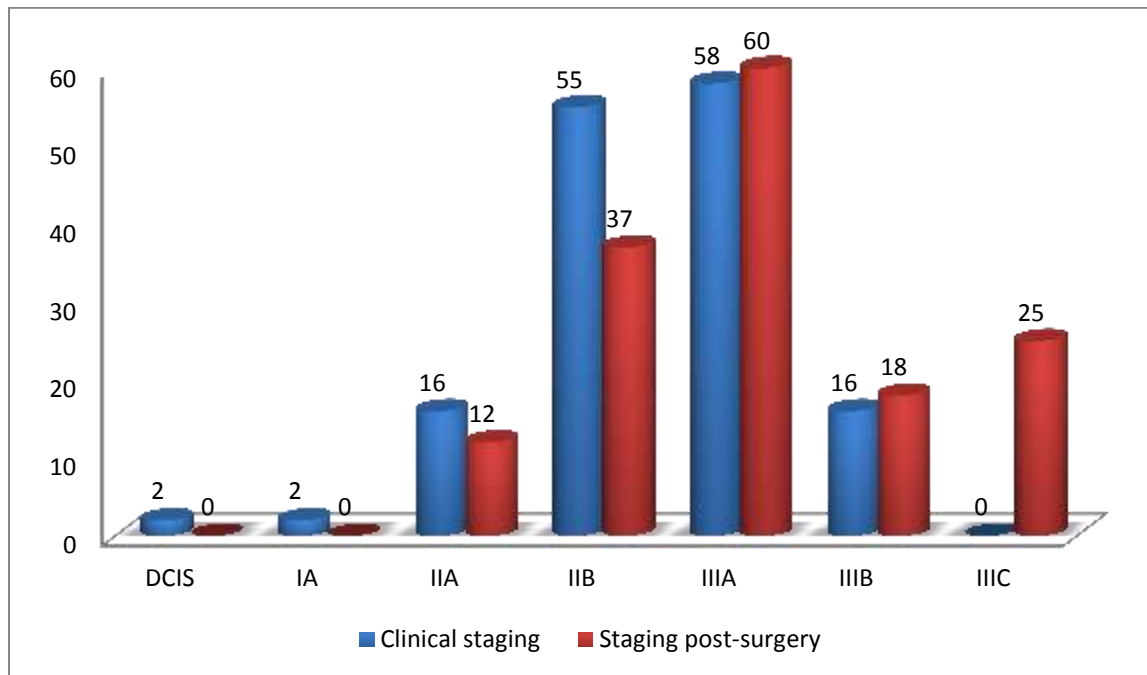
Parameter	Number	Percentage
Comorbid illness		
Type2 Diabetes Mellitus	54	36
Systemic Hypertension	48	32
Pre-existing lung disease		
Bronchial asthma	8	5
Old pulmonary khocs	2	<2
Side of treatment		
Right	75	49
Left	77	51



IDC- Infiltrating ductal carcinoma, ILC- Infiltrating Lobular carcinoma, Mixed- IDC+ILC, IMC- Infiltrating mammary carcinoma, NEF- Neuro endocrine features, LC NEC- Large cell Neuro endocrine carcinoma, Miscellaneous- Poorly differentiated carcinoma, mucinous carcinoma, metaplastic carcinoma, medullary carcinoma.



## AJCC Staging



3 patients underwent mastectomy outside

Patient characteristics (Patient factor- Lung volume in cc)

	Mean	Minimum	Maximum
Lung on irradiated side	892	469	1452
Lung on opposite side	852	474	1635
Right lung	925	474	1635
Left lung	751	469	1452
Total lung volume	1744	1102	3087

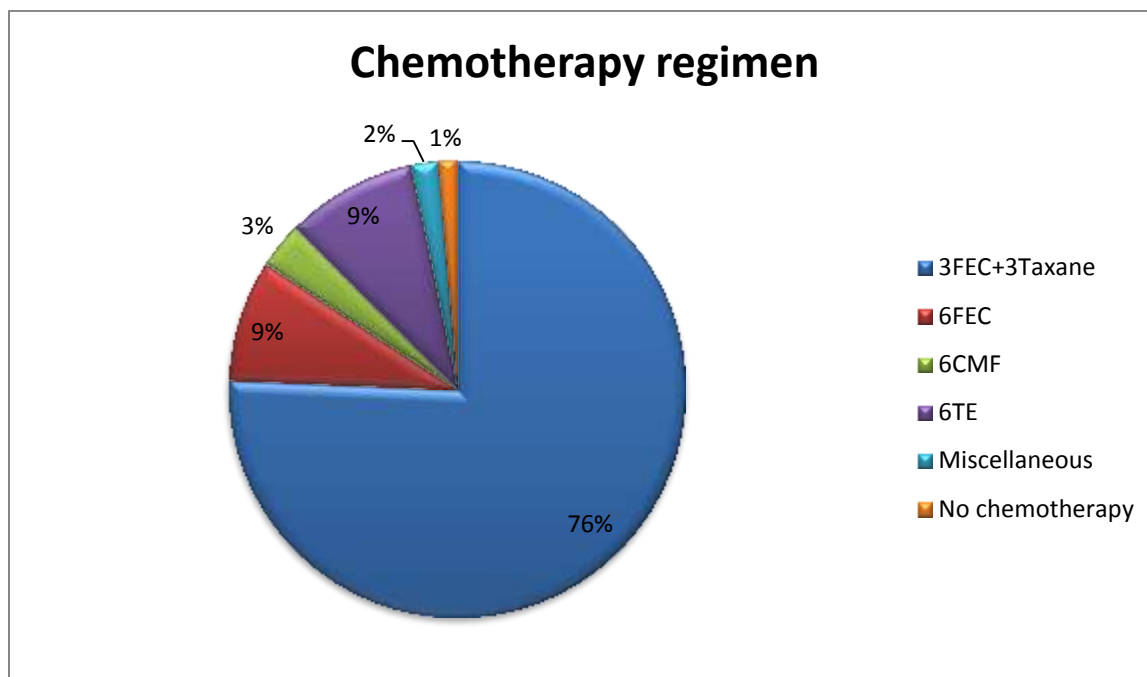
## **Treatment**

Early breast cancer patients stage IIA and IIB underwent straight surgery, Either breast conservation surgery (Excluded from the study) or modified radical mastectomy. Stage IIIA and IIIB patients receive neoadjuvant chemotherapy followed by mastectomy. All patients who received neoadjuvant chemotherapy received 2 to 3 cycles chemotherapy prior to surgery and complete chemotherapy after surgery. All patients received 6 cycles of chemotherapy except 2 patients who were not considered for chemotherapy in view of comorbid illness. All patients for whom post mastectomy radiation is indicated received post mastectomy LRRT sequentially 3 to 4 weeks after completion of all 6 cycles of chemotherapy or once wound is fit when chemotherapy is not considered. (Patients with supraclavicular, internal mammary nodes, margin positivity were excluded from my study). If patient is receptor positive hormones were given after completion of radiation. All premenopausal women received Anti oestrogen (Tamoxifen 20 mg PO OD) and postmenopausal women received Anastrozole inhibitor (Letrozole 2.5 mg PO OD) Perimenopausal women underwent hormonal assays and received hormonal therapy accordingly. Premenopausal women on Tamoxifen were offered bilateral salphingo opherectomy if they resumed menstruation at follow up and hormones changed accordingly.

## Treatment details

Sequencing of treatments	number	Percent
Upfront surgery followed by adjuvant treatments	89	59
Neoadjuvant chemotherapy followed by surgery and completion of chemotherapy / other adjuvant treatments	63	41

2 patients had concurrent chemoradiation (Post mastectomy)



2 patients had no chemotherapy, 1 patient had 3FEC+3 Paclitaxel, 1 patient had 1TEF (OS) +2FEC+3DOC

Miscellaneous 6EC (Epirubicin/Cyclophosphamide), 6EP (Etoposide/Cisplatin), 3FEC+3TE

## Chemotherapy regimens used

### i) 3FEC+ 3Taxane

Injection 5FU at a dose of 600 mg/m<sup>2</sup> as IV Bolus on D1

Injection Epirubicin at a dose of 90 mg/m<sup>2</sup> as IV bolus on D1

Injection Cyclophosphamide at a dose of 600 mg/m<sup>2</sup> as IV infusion D1

of a 21 day cycle for 3 cycles followed by

Injection Docetaxel at a dose of 75 mg/m<sup>2</sup> as IV infusion on D1

of a 21 day cycle for 3 cycles.

### ii) 6FEC

Injection 5FU at a dose of 600 mg/m<sup>2</sup> as IV Bolus on D1

Injection Epirubicin at a dose of 90 mg/m<sup>2</sup> as IV bolus on D1

Injection Cyclophosphamide at a dose of 600 mg/m<sup>2</sup> as IV infusion D1

of a 21 day cycle for 6 cycles

### iii) 6CMF

Injection Cyclophosphamide at a dose of 600 mg/m<sup>2</sup> as IV infusion D1

Injection methotrexate at a dose of 50 mg/m<sup>2</sup> as IV bolus on D1

Injection 5FU at a dose of 600 mg/m<sup>2</sup> as IV Bolus on D1

of a 21 day cycle for 6 cycles

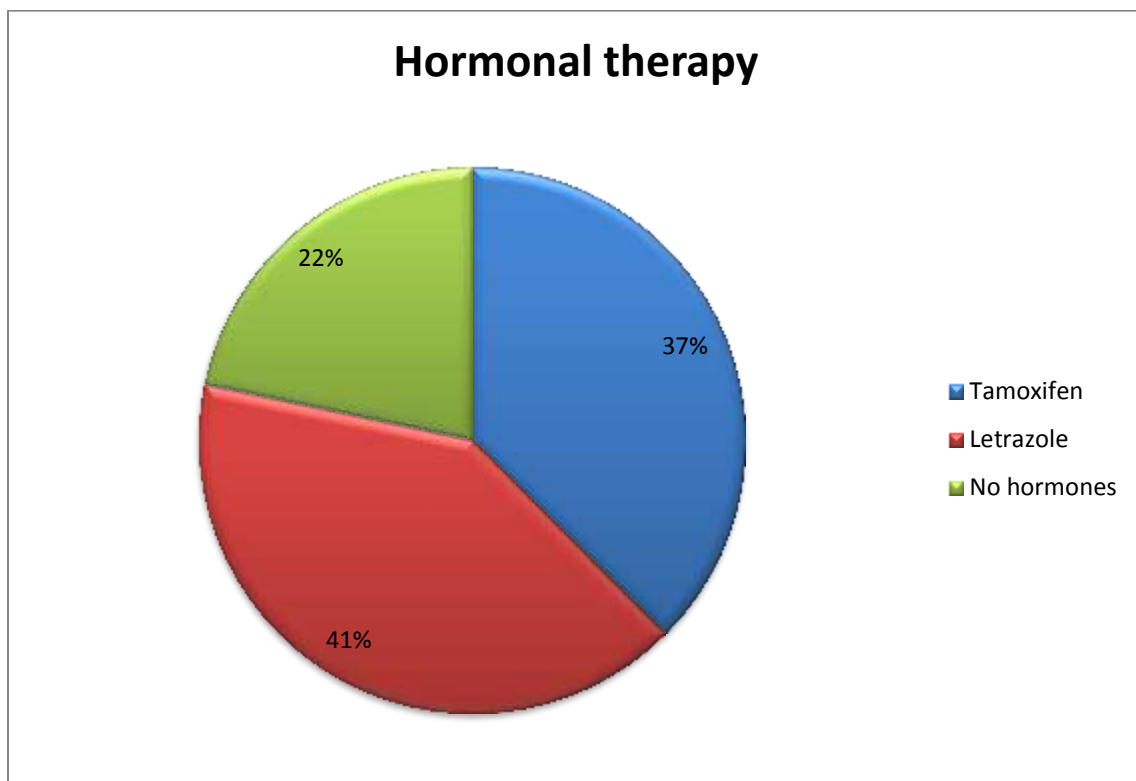
iv) 6 TE

Injection Paclitaxel at a dose of 175 mg/m<sup>2</sup> as IV infusion on D1

Injection Epirubicin at a dose of 60 mg/m<sup>2</sup> as IV bolus on D1

of a 21 day cycle for 6 cycles

### Hormonal therapy



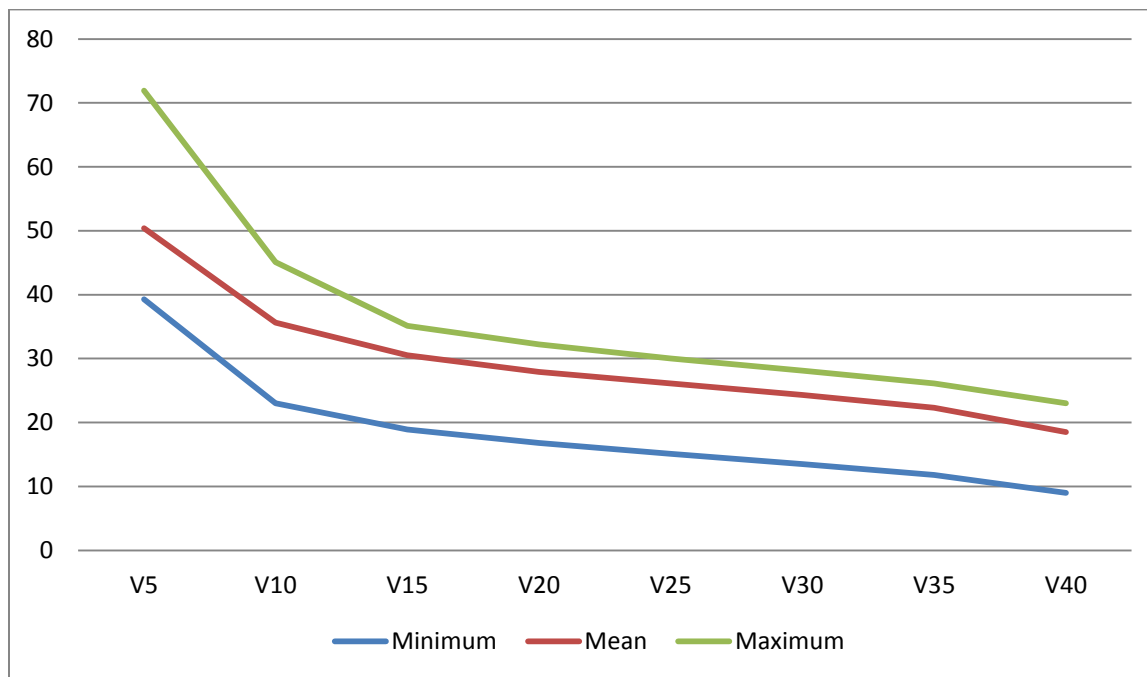
A post-menopausal lady had brugada syndrome and was given tamoxifen as letrozole is associated with increased cardiac risk.

## DVH PARAMETERS

2 D parameters n=152

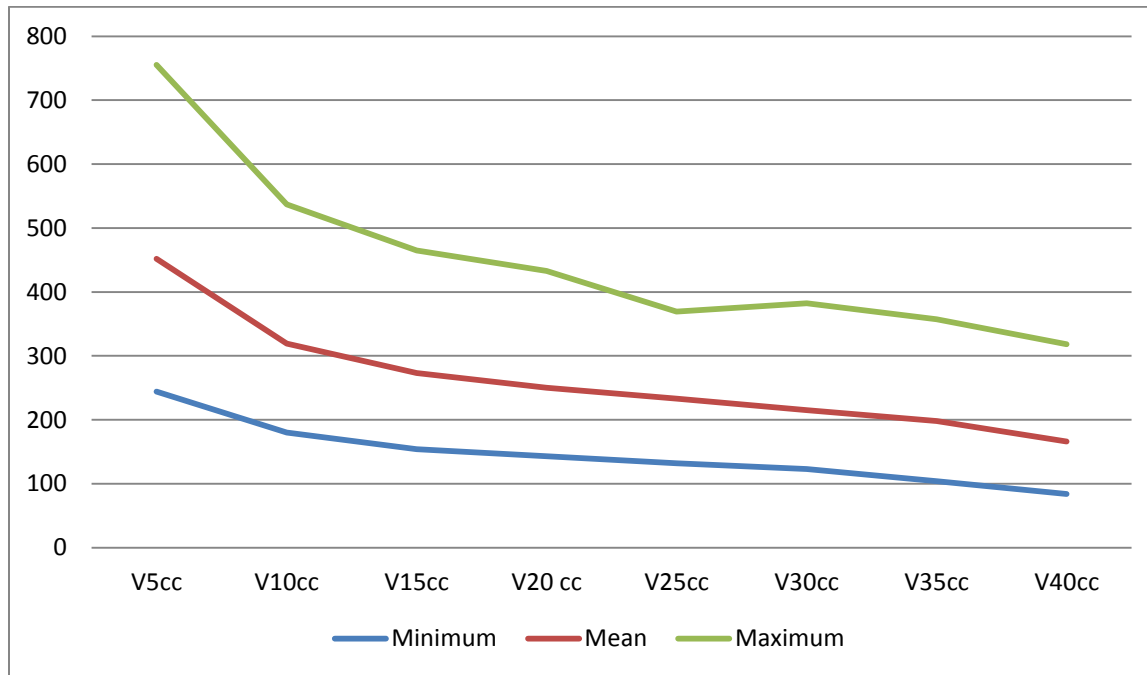
Parameter	Lung length (cm)	Central lung distance (cm)	Maximum Lung distance (cm)	Average lung Distance (cm)
Minimum	10.45	1.39	2.28	1.76
Maximum	20.02	5.07	5.27	3.7
Mean	14.54	2.8	3.15	2.68

Relative lung volumes irradiated n=152



Parameter	V5%	V10%	V15%	V20%	V25%	V30%	V35%	V40 %
Minimum	39.3	23	18.9	16.8	15.1	13.5	11.8	9
Maximum	71.9	45.1	35.1	32.2	30.0	28.1	26.1	23
Mean	50.4	35.6	30.5	27.9	26.1	24.3	22.2	18.5

### Absolute lung volumes irradiated n=152



Parameter	V5cc	V10cc	V15cc	V20cc	V25cc	V30cc	V35cc	V40cc
Minimum	244	180	154	143	132	123	104	84
Maximum	755	537	465	433	369	382	357	318
Mean	452	319	273	250	233	215	198	166

### Lung doses n=152

Parameter	D25 (Gy)	Minimum Lung dose (Gy)	Maximum Lung dose (Gy)	Mean Lung dose (Gy)
Minimum	5.2	0.00	12.33	6
Maximum	37	0.78	80.00	21.50
Mean	28	0.42	49.88	14.48

## **RADIATION PNEUMONITIS**

### **Symptomatic Radiation pneumonitis (SRP)**

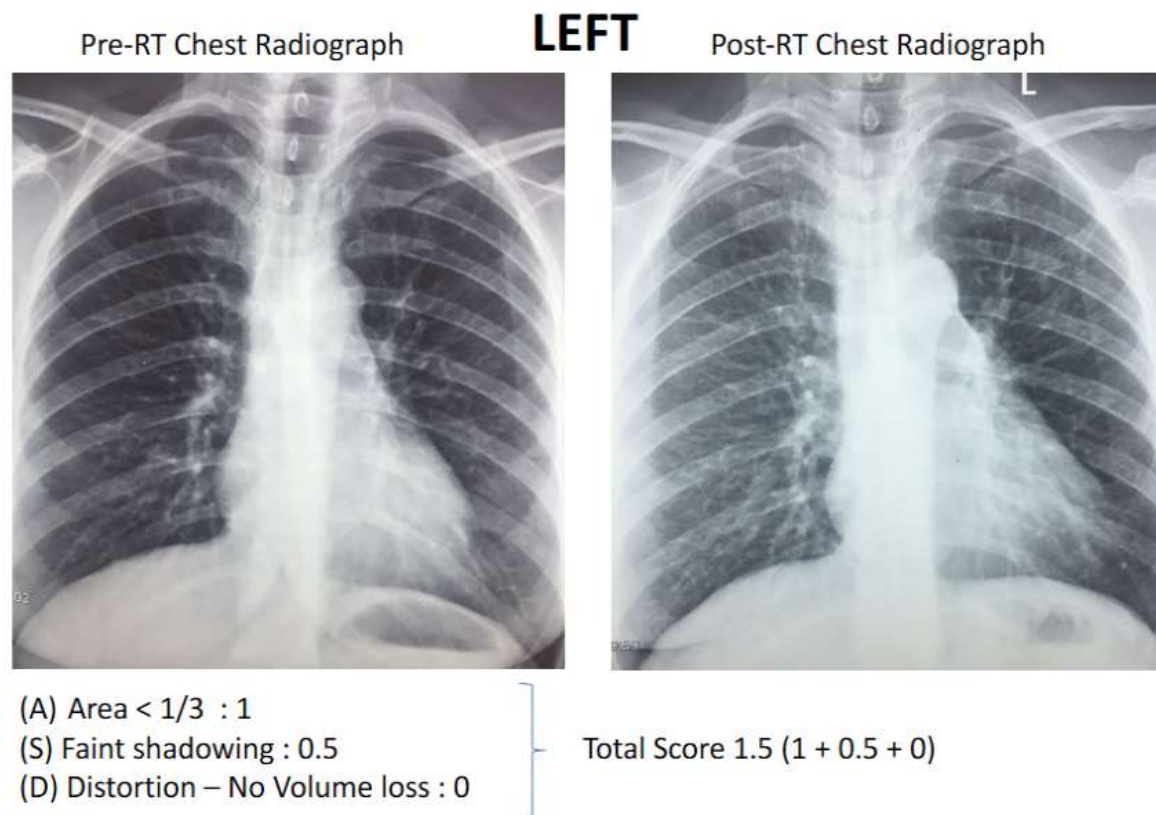
Only 2 patients had dry cough requiring antitussives during RT, which subsided almost within one week and remained asymptomatic for rest of their treatment course and follow up, chest x ray done was normal and they scored zero for radiological pulmonary toxicity after completing one year of follow up. One patient developed cough 6 months post completion of RT subsided with a course of antibiotics and mucolytic, chest x ray done at that time was normal and one year follow up chest x ray was also scored zero. None of them was suspected to have radiation pneumonitis.

### **Radiological Pulmonary Toxicity (RPT)**

26 patients had radiological pulmonary changes when scored using modified WHO grading system for radiographic pulmonary toxicity. That is, an incidence of 17.1%. None of these 26 patients had any symptoms. Two patients had radiological changes in the region corresponding to SCL field and in rest of the 24 patients radiological changes correspond to Tangential field. 19 patients had a score of 1.5, 4 patients had a score of 2 and one each had a score of 2.5, 3 and 5. Shown below are a few Chest radiographs of patients who showed Radiographic changes. Chest radiograph prior to radiation is shown on the left hand side and



chest radiograph one year post radiation on the right hand side. Modified WHO grading for RPT score and the description of changes seen are given below each set.



Patient irradiated on left side. Faint shadowing left upper zone with patchy opacity with no volume loss

Pre-RT Chest Radiograph

**RIGHT**

Post-RT Chest Radiograph



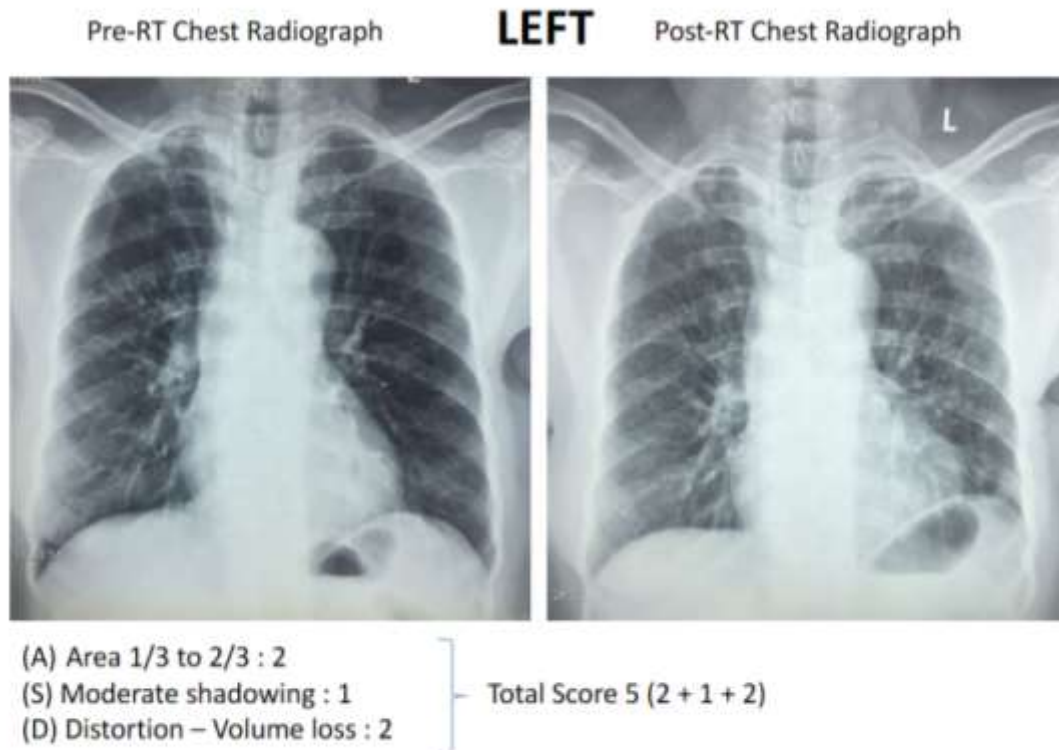
(A) Area 1/3 to 2/3 : 2

(S) Moderate shadowing : 1

(D) Distortion – No Volume loss : 0

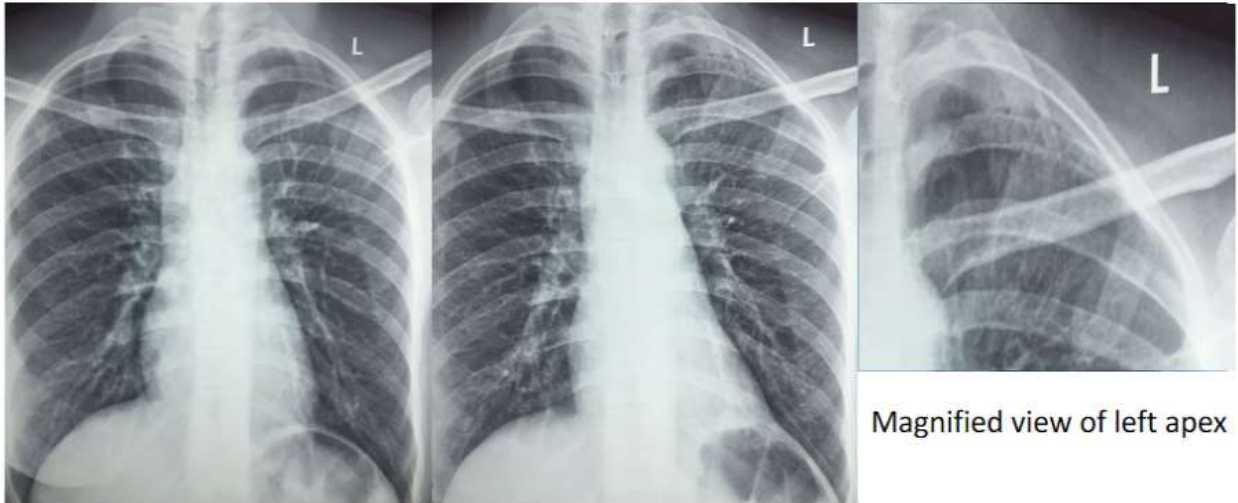
Total Score 3 (2 + 1 + 0)

Patient irradiated on right side. Ill-defined scattered patchy infiltrates in Right mid and lower zones, Focal right pleuro-diaphragmatic adhesions are seen with moderate shadowing. No volume loss.



Patient irradiated on left side. Moderate shadowing seen in Left Upper, Mid and Lower zone. Left diaphragmatic elevation with obliteration of costo-phrenic angle and volume loss.

Pre-RT Chest Radiograph **LEFT** Post-RT Chest Radiograph



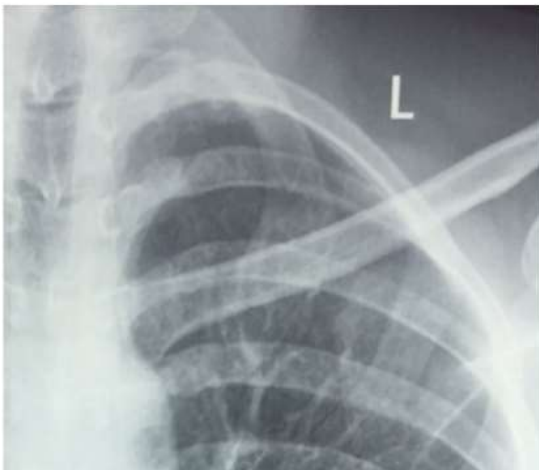
(A) Area  $< 1/3$  : 1  
 (S) Faint shadowing : 0.5  
 (D) Distortion – No Volume loss : 0

} Total Score 1.5 (1 + 0.5 + 0)

Patient irradiated on left side. Apical fibrotic scarring and pleural thickening seen in left lung.

#### MAGNIFIED VIEW

Pre-RT Chest Radiograph



Post-RT Chest Radiograph



Pre-RT Chest Radiograph **LEFT** Post-RT Chest Radiograph



(A) Area  $<1/3$ : Score 1

(S) Faint shadowing : Score 0.5

(D) Distortion- No volume loss: Score 0

Total score  $(1+0.5+0)= 1.5$

Patient irradiated on left side. Apical fibrotic scarring left lung apex.

#### MAGNIFIED VIEW

Pre-RT Chest Radiograph

Post-RT Chest Radiograph



### **3.b STATISTICAL ANALYSIS**

#### **FACTORS AND CORRELATION**

Among the patient factors Age showed a strong positive association with development of radiologic pulmonary toxicity. RPT

Age was strongly associated with RPT (27.1% in patients 50 years and older, 4.5 % in patients less than 50 years of age  $p<0.001$ . Similarly, 36.4 % in patients 60 years and older, 11.8 % in patients less than 60 years  $p=0.004$ ) with increasing incidence as age increases. Number of patients who received treatment on right side are 75 and on left side are 77. Right sided treatments were less associated with RPT compared to Left ( $p= 0.037$ )

No significant association was seen with BMI (Mean BMI without RPT  $26.12 \pm 6.11$  and with RPT  $26.21 \pm 5.57$ ,  $p=0.95$ )

Factor	Radiological Radiation Pneumonitis						
	YES		NO		Total		p
	N	%	N	%	N	%	Value
Age $\geq$ 50 yrs	23	27.1	62	72.9	85	100	p<0.01
Age < 50 yrs	3	4.5	64	95.5	67	100	
Total	26	17.1	126	82.9	152	100	
Age $\geq$ 60 yrs	12	36.4	21	63.3	33	100	p=0.04
Age < 60 yrs	14	11.8	105	88.2	119	100	
Total	26	17.1	126	82.9	152	100	
Left	18	23.4	59	76.6	77		p=0.037
Right	8	10.7	67	89.3	75		
Total	26	17.1	126	82.9	152	100	
Smoking/Passive smoking	14	45.2	17	54.8	31		p<0.01
No exposure	12	10.1	109	89.9	121		
Total	26	17.1	126	82.9	152	100	
Bronchial Asthma	4	50	4	50	8		p=0.012
Normal	22	15.4	122	84.6	144		
Total	26	17.1	126	82.9	152	100	

## TREATMENT RELATED FACTORS

Though all patients who received chemotherapy completed 6 cycles and were started on radiation 3 to 4 weeks after completion of radiation, RPT in patients who received neo adjuvant chemotherapy and had a break in chemotherapy in view of surgery and then completed rest of the chemotherapy and in patients who underwent upfront surgery and received all 6 cycles chemotherapy at a stretch as adjuvant treatment was analysed and found to have no significant association with RPT (RPT seen in 16.3% patients who received all 6 cycles without interruption and 17.5 % in patients who had a break due to surgery,  $p=0.958$ ). 2 patients did not receive chemotherapy and one of the two developed RPT.

### Type of chemotherapy

When broadly divided into 4 groups, patients who received 3FEC+3DOC, 6FEC, 6CMF and 6TE association with RPT was found in 15.8% (18/114), 8.3% (1/12), 60% (3/5) and 21.14% (3/14) respectively,  $p=0.06$  (not significant).



## Hormonal therapy

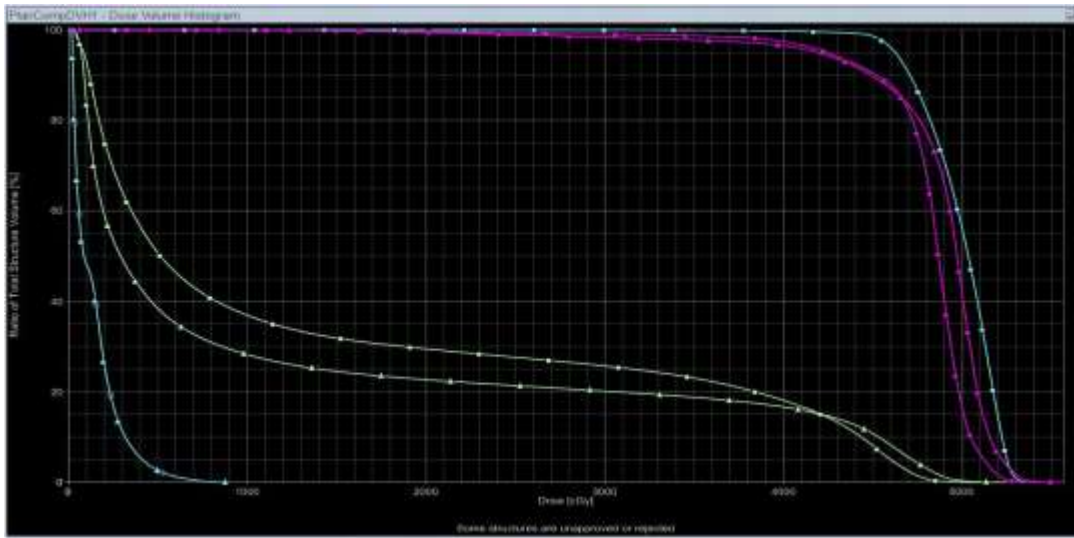
	Radiation pneumonitis (RPT)						
	Present		Absent		Total		p value
	N	%	N	%	N	%	P=0.05
No hormones	5	14.7	29	85.3	34		
Tamoxifen	5	9.1	50	90.9	55		
Letrozole	16	25.8	47	74.2	63		
Total	26	17.1	126	82.9	152	100	

## DVH FACTORS

No significant association of RPT with Total volume of lung on the treated side (Mean volume without RPT 927.9 cc and with RPT 884.8 cc,  $p=0.252$ ), Mean lung dose (Without RPT 14.4 Gy and with RPT 15.0 Gy,  $p=0.129$ ), Maximum Lung dose (Without RPT 49.8 Gy and with RPT 50.5 Gy,  $p=0.403$ ), Lung length LL (Without RPT  $14.46 \pm 1.52$  cm and with RPT  $15.03 \pm 2.46$  cm,  $p=0.296$ ), Central Lung Distance CLD (Without RPT  $2.90 \pm 0.53$  cm and with RPT  $2.91 \pm 0.56$  cm,  $p=0.978$ ), Average Lung Distance (Without RPT  $2.67 \pm 0.35$  cm and with RPT  $2.71 \pm 0.43$  cm,  $p=0.729$ ), Maximum Lung Distance (Without RPT  $3.3.21 \pm 0.47$  cm and with RPT  $3.23 \pm 0.66$  cm,  $p=0.890$ ) Relative and Absolute Lung volumes irradiated was seen.

## IMPACT OF SCL FIELD

For 30 random patients second plan was made by removing the SCL field and a compound DVH was generated to analyse the impact of SCL field. All DVH parameters were noted and analysed.



Compound DVH of a patient showing the doses received by the lung on the treated side with and without SCL field. Pink line is for the Target volume, Blue line is for SCL region and cyan line for Lung. Lines are marked with arrow heads for the doses generated when SCL field is removed and with Squares for doses generated with SCL included. Equivalent Uniform Dose (EUD) is derived from the DVH and Normal Tissue Complication Probability (NTCP) calculated using EUD based MATLAB program [52]. Mean NTCP with SCL and without SCL field are 0.37% and 0.75 % respectively. There was only a weak positive correlation of NTCP with RPT.

Mean of relative lung volumes irradiated n=30

Parameter	V5	V10	V15	V20	V25	V30	V35	V40
With SCL field	51.1	36.0	30.8	28.4	26.4	24.7	22.4	18.8
Without SCL field	43.0	31.6	27.4	25.2	23.5	22.1	20.4	17.9

Mean of Absolute lung volumes irradiated n=30

Parameter	V5cc	V10cc	V15cc	V20cc	V25cc	V30cc	V35cc	V40cc
With SCL field	467	329	282	259	241	226	206	173
Without SCL field	394	289	250	230	215	202	188	165

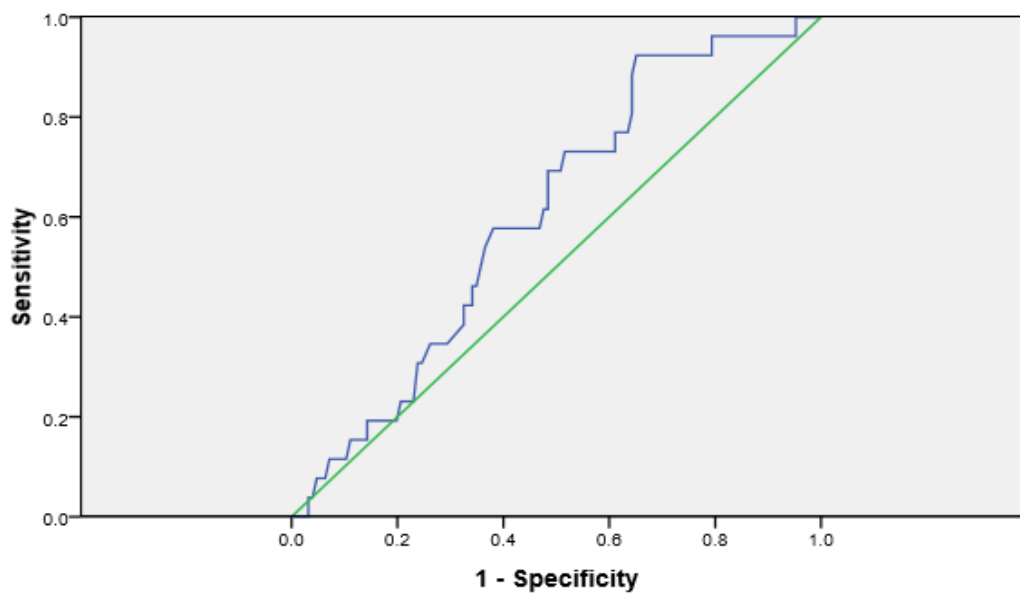
Mean of Lung doses n=30

Parameter	D25	Minimum Lung dose Gy	Maximum Lung dose Gy	Mean Lung dose Gy
With SCL field	29.3	0.43	50.6	14.8
Without SCL field	27.4	0.42	51.7	13.1

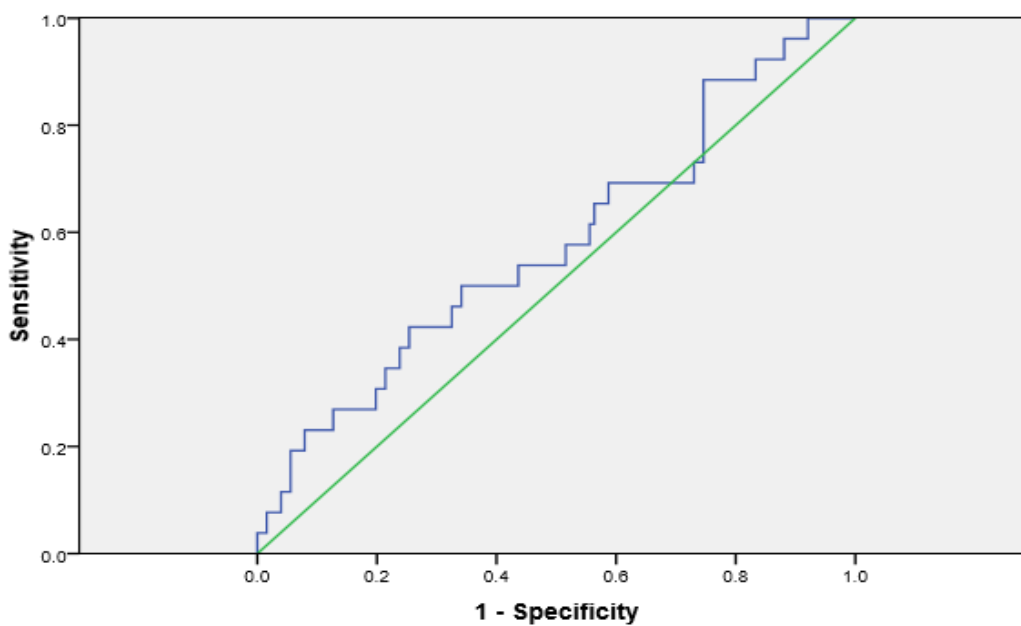
SCL region was treated with Single Direct anterior oblique field in 53 (35%) patients and an addition posterior boost in 99 (65%) patients. Minimum, Maximum and Mean Apical lung distance are 0.33 cm, 3.64 cm and 1.99 cm respectively.

Only 2 patients developed apical RPT Apical lung distance in them was 2.92 and 3.14. One of them treated with Single direct oblique field alone and the other had an additional posterior boost field for SCL

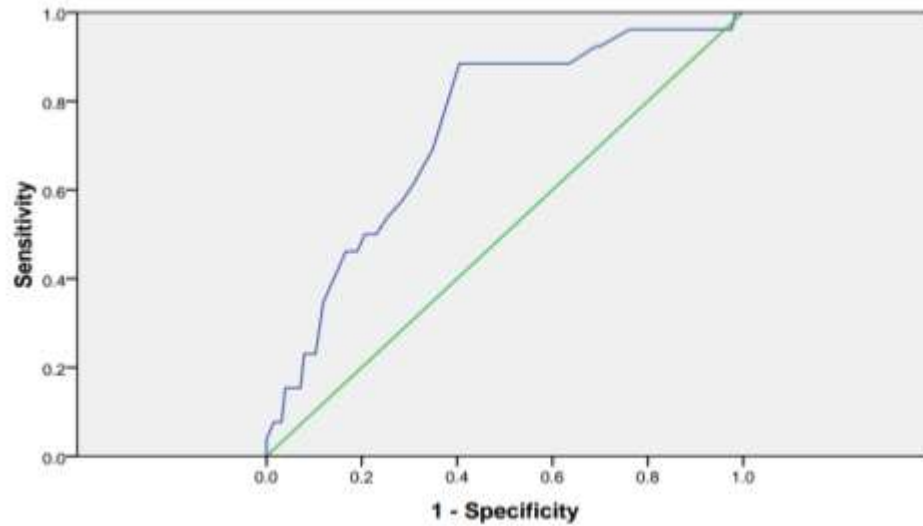
## ROC curves



ROC for development of RPT with V 20 (relative) AUC 60.5 p= 0.432



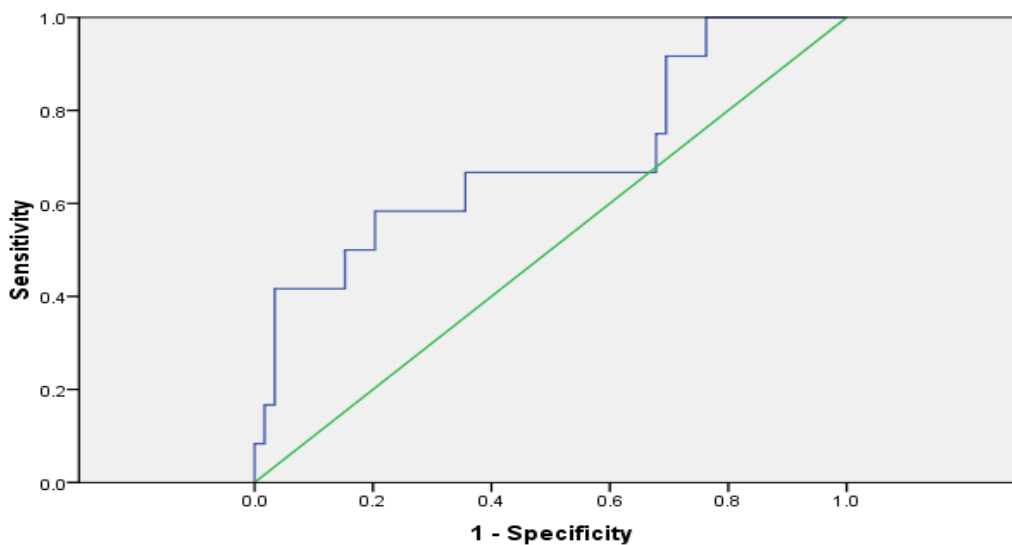
ROC for development of RPT with V20 cc (absolute) AUC 57.9 p=0.207



ROC for development of RPT with Age

Proposed cut off with ROC for Age 50 years with a sensitivity of 90% and specificity of 60% (AUC 75.8  $p = 0.01$ )

ROC for the 30 cases for whom a second plan without SCL field is generated



Proposed cut off with ROC for absolute volume of lung receiving 20 Gy and more is 278.6 cc with a sensitivity of 40% and specificity 90% (AUC 69.5  $p = 0.034$ )

#### **IV. DISCUSSION**

Due to increasing awareness and wide spread use of screening mammography there is an increase in incidence, more so of early breast cancers. With improved understanding of the disease and better treatment options now available there is an increase in life expectancy of breast cancer patients. The trend is changing to more limited surgeries to reduce morbidity (eg, BCS) with more indications for radiation. Also there is changing trend towards limited axillary dissections with indications for radiation to address axillary region. All these have led to changing guidelines with increased scope of radiation by identifying subgroups who will benefit from radiation. Hence, more patients are being considered for adjuvant radiation treatment. Improved techniques of radiation have facilitated to decrease radiation morbidity without compromising dose to target volumes. Breast cancer patients receiving post mastectomy radiation form a large group among the patients receiving radiation close to lung and PMRT being adjuvant treatment in long term survivors; the incidence and intensity of complications have to be kept as low as possible. Improved radiation techniques like three-dimensional conformal radiotherapy (3D-CRT) have made it possible to limit the amount of incidentally irradiated lung volume.

Incidence of radiological radiation pneumonitis in this study is 17.1 % and none of the patients had symptomatic radiation pneumonitis. These findings are

consistent with the impression of most radiation oncologists that radiation to breast cancer patients is well tolerated with a very low incidence of radiation pneumonitis. Pneumonitis after conformal radiotherapy in other studies range from 0.9% - 47 % (RPT 6.4% to 87%).

Study (Number /Year)	Type	Treatment	Target volume	Chestwall	TD
U. Blom Goldman et al. [7] (89/ 2014)	Prospective MRM/BCS	3D Conformal with V20 contstraint < 30%	Chest wall/ breast +IMR $\pm$ SCL	Electrons	46
Pehr ARM Lind et al [13] (177 / 1997)	Retrospective MRM	CT based planning	CW+IMR+SC L	Electrons	46
	BCS		CW+Breast+I MR	Photons	50
Zsuzsanna Kahan et al [8] (119/2007)	Prospective	CT based treatment planning	CW/Breast+ IMR $\pm$ SCL	Photons	46-50
Tatiain et al [9] (1624/1991 )	Retrospective	-	Breast	Photons	-
Cem onal et al [10] (122/2012)	Retrospective	Conformal	CW/Breast $\pm$ IMR $\pm$ SCL	Electrons/ Photons	50
Hak Jae kim et al [11] (261/2009)	Retrospective	3D RT planning	CW/Breast $\pm$ SCL	Photons	50.4
Sung ho moon et al [31] (171/2007)	Retrospective	Conformal	CW/Breast $\pm$ SCL	Photons	50.4

Study (Number /Year)	Tools	Symptomatic radiation pneumonitis	Radiological radiation pneumonitis	Assesment time
U. Blom Goldman et al. [7] (89/ 2014)	PFT CTC criteria	4 mild 1 moderate	-	1/4/7 months
Pehr ARM Lind et al [13] (177 / 1997)	Clinical assesment	MRM 24% 14% steroid BCS 50% 22%	-	1-7 months
Zsuzsanna Kahan et al [8] (119/2007	Clinical assesment CT chest- Mean density changes TGF $\beta$	7.5% early	34% early Late 35.4%	3/12 months
Tatian et al [9]	Clinical assessment and chest radiograph	Over all 1% (17) Sequential CT 1.3% Concurrent CT 8.8%	All patients with symptoms (5 patients had permanen scaring)	1-12 months
Cem onal et al [10] (122/2012)	Clinical assesment RTOG toxicity criteria	Grade 3- steroid requiring pneumonitis 4 4 field 1 2 field	-	6 months
Hak Jae kim et al [11] (261/2009)	Clinical assessment RTOG grade 2 and higher chest radiographs	1.9%	22.6%	Every 3 months andcxr at 1 year
Sung ho moon et al [31] (171/2007)	Clinical assesment RTOG toxicity criteria serial chest radiographs	2.1%( 3 grade 3 one grade 2)	13.9 % tangential field teritory (137) 49.2% SCL field teritory (59)	Every 3 months and one year



## PATIENT FACTORS

Age is a patient factor which is found to have significant positive association with RPT. This is consistent with various other similar studies. Patients older than 60 years had a 3 times increased risk of developing RPT. Proposed cut off with ROC is 50 years with a sensitivity 90% and specificity 60% for developing RPT.

Patients who received treatment on the right side are less associated with development of RPT compared to left side. Left side development of RPT was twice more common compared to the right side which may be attributed to the lesser mean lung volume on left side 751 cc leading to more absolute lung volume irradiated compared with right using same constraints for both the sides.

With a constraint of  $V20 \leq 30\%$  and Mean lung dose  $\leq 15$  Gy no association is found for Lung volume irradiated and lung doses with RPT. However, Bilateral total lung volume has significant positive association with the development of RPT (Difference in means of total bilateral lung volume with and without RPT are 1906.5 cc and 1710 cc) which may be due to more absolute lung volume being irradiated in larger lungs when a relative lung volume is used as the constraint.

Patients exposed to passive smoking/ had a habit of tobacco chewing had 4 times increased association with RPT compared to patients with no exposure.

Patients with bronchial asthma had 3 times increased association with RPT compared to patients with normal airways

Only two patients had history of treated pulmonary tuberculosis none of them developed neither symptomatic nor radiological pneumonitis.

## TREATMENT FACTORS

All patients received only sequential radiation and radiation was started within 4 to 6 weeks of completing chemotherapy

### Type of chemotherapy

CMF- both cyclophosphamide and methotrexate are known to cause pulmonary toxicity by local inflammation. The higher association, though not significant, with CMF chemotherapy (3 out of 5 patients) can be attributed to the age of patients receiving CMF chemotherapy, usually elderly. Mean age of patient who received CMF 64.8 years

## Hormonal therapy

Paradoxically, tamoxifen seems to be associated with reduced RPT compared to no hormonal therapy and letrozole is associated with increased RPT. (Mean age of patients not on hormones, on tamoxifen and on letrozole are 50 yrs, 43 yrs and 57 yrs respectively) This higher association of RPT with letrozole can be again attributed to the age of patients receiving letrozole.

On applying logistic regression age is found to be an independent risk factor irrespective of hormonal therapy or chemotherapy received by the patient.

## DVH - PARAMETERS

Constraint for lung doses used were  $V20 \leq 30\%$  and Mean lung dose  $\leq 15$  Gy. Mean V20 (relative), V20 (absolute) and MLD are 27.9%, 250 cc and 14.48 Gy respectively in the study population.

There was no significant association of RPT with any of DVH parameters 2D / Relative / Absolute lung volumes irradiated. ROC curves were generated by no threshold /cut off could be obtained. But, ROC curves in the subset of population studied for the impact of SCL showed a cut off for absolute lung volume irradiated to be less than 278 cc.

## V. CONCLUSION

The incidence of pneumonitis in patients treated with post mastectomy loco regional radiation is very less with no documented symptomatic pneumonitis and only 17.1 % Radiological Pulmonary Toxicity at a median follow up of 21 months. Age is the single most significant associated factor. Patients with age more than 60 years have 3 fold increased risk. Other factors associated with increased risk of development of RPT are exposure to smoking and bronchial asthma. Side of treatment to be taken into account as lung volumes vary with the side. With a lung constraint of  $V20 \leq 30\%$  and Mean lung dose of  $\leq 15$  Gy, LRRT (Chest wall including IMN region and SCL field) using conformal therapy, total dose of 46 Gy (daily dose of 180 cGy), can be given safely.

Prospective studies with more sensitive tools CT and additional PFT are required as consensus guidelines regarding factors responsible for radiation pneumonitis are not available.

## VI. REFERENCES

1. Ahmedin Jemal, Freddie Bray, Melissa M et al, **Global Cancer Statistics**, *Ca Cancer J Clin* 2011;61:69–90.
2. J Ferlay, Soerjomataram, R Dikshit et al, **GLOBOCAN 2012: Estimated cancer incidence, mortality and prevalence**, *International Agency for Research on Cancer*, Lyon, France (WHO)
3. Shantha V, Swaminathan R, Balasubrahmanyam, **Cancer Incidence and mortality in Chennai**, India 2012-14, *MMTR*.
4. Lori J. Pierce, **The use of radiotherapy after mastectomy: A review of the literature**, *J Clin Oncol* 23: 1706-1717.
5. P.M. Poortmans et al, **Internal Mammary and Medial Supraclavicular Irradiation in Breast Cancer** *N Engl J Med* 2015;373:317-27.
6. U. Blom Goldman et al, **Radiation pneumonitis and pulmonary function with lung dose-volume constraints in breast cancer irradiation**, *Journal of Radiotherapy in practice* (2014) 13,211-217.
7. Ulla Blom Goldman et al, **Reduction of radiation pneumonitis by V20 constraints in breast cancer**, *Radiation Oncology* 20105:99.
8. Zsuzanna kahan et al, **The risk of early and late lung sequelae after conformal radiotherapy in breast cancer patients**, *Int. J. Radiation Oncology Biol. Phys.*, Vol. 68, No. 3, pp. 673–681, 2007.
9. Tatiana I et al, **Radiation pneumonitis in breast cancer patients treated with conservative surgery and radiation therapy**, *Int. J. Radiation Oncology Biol. Phys.*, Vol. 21, pp. 355-360.
10. Cem Onal et al, **Correlation of Conventional and Conformal Plan Parameters for Predicting Radiation Pneumonitis in Patients Treated with Breast Cancer**, *J Breast Cancer* 2012 September; 15(3): 320-328.

- 11.Hak Jae Kim et al, **Radiation- induced Pulmonary Toxicity and related risk factors in breast cancer**, *Journal of breast cancer* 2009 june; 12 (2): 67-72.
- 12.Tae Hyun Kim et al, **Dose-volumetric Parameters for Predicting Severe Radiation Pneumonitis after Three dimensional Conformal Radiation Therapy for Lung Cancer**, *Radiology* 2005; 235:208–215.
- 13.Pehr A.R.M Lind et al, **A Descriptive Study of Pulmonary Complications After Postoperative Radiation Therapy in Node-Positive Stage II Breast Cancer**, *Acta Oncologica* Vol 36, No. 5. pp. 509-515. 1997.
- 14.Effect of radiotherapy after mastectomy and axillary surgery on 10-year recurrence and 20-year breast cancer mortality: meta-analysis of individual patient data for 8135 women in 22 randomised trials **EBCTCG (Early Breast Cancer Trialists' Collaborative Group)** *Lancet* 2014; 383: 2127–35.
- 15.Timothy J. Whelan et al, **Regional Nodal Irradiation in Early-Stage Breast Cancer**, *N Engl J Med* 373;4 nejm.org July 23, 2015.
- 16.NCCN guidelines version 2 2016.
- 17.**Oncology Clinical Service Line System-wide Consensus Guidelines: Postmastectomy Radiation for Patients with 1-3 Positive Lymph Nodes.** Virginia piper cancer institute, *Allina health breast program*.
- 18.Ibrahim Awad, et al. **Moving from 2D to 3D-CRT Planning of Chest Wall for Post mastectomy Breast Cancer Patients: Mansoura University Experience**, *Med. J. Cairo Univ.*, Vol. 81, No. 1, March: 21-27, 2013.
- 19.Salah El-Mesidy, **Dosimetric comparison of Intensity-Modulated Radiation Therapy (IMRT) vs. 3D Conformal Radiotherapy (3D-CRT) in operable breast cancer**, *Pan Arab Journal of Oncology*, vol 4; issue 4, December 2011.

20. Pierce LJ, Butler JB, Martel MK, et al: **Post mastectomy radiotherapy of the chest wall: Dosimetric comparison of common techniques.** *Int J Radiat Oncol Biol Phys* 52:1220-1230, 2002
21. Pierce et al, **Post mastectomy radiotherapy of the chest wall: Dosimetric comparison of common techniques,** *Int. J. Radiation Oncology Biol. Phys.*, Vol 52, No 5, Pg 1220-1230, 2001.
22. Marks et al, 2060 **Radiation (RT) induced pneumonitis following tangential breast/chestwall irradiation,** *Int. J. Radiation Oncology Biol. Phys.*, Volume 48, Number 3, Supplement, Pg 294-295, 2000.
23. Lingos TI, Recht A, Vicini F, et al: **Radiation pneumonitis in breast cancer patients treated with conservative surgery and radiation therapy.** *Int J Radiat Oncol Biol Phys* 21:355-360, 1991.
24. Tse-Kuan Yu et al, **Clinically Relevant Pneumonitis After Sequential Paclitaxel-Based Chemotherapy and Radiotherapy in Breast Cancer Patients,** *Journal of the National Cancer Institute*, Vol. 96, No. 22, November 17, 2004.
25. Alphonse G. Taghian et al, **Risk of Pneumonitis in Breast Cancer Patients Treated with Radiation Therapy and Combination Chemotherapy With Paclitaxel,** *Journal of the National Cancer Institute*, Vol. 93, No. 23, December 5, 2001.
26. Hojris I, Andersen J, Overgaard M, et al: **Late treatment-related morbidity in breast cancer patients randomized to post mastectomy radiotherapy and systemic treatment versus systemic treatment alone.** *Acta Oncol* 39: 355- 372, 2000.
27. Hanna YM, Baglan KL, Stromberg JS, et al: **Acute and subacute toxicity associated with concurrent adjuvant radiation therapy and paclitaxel in primary breast cancer therapy.** *Breast J* 8:149-153, 2002.

28. **Is a reduction in radiation lung volume and dose necessary with paclitaxel chemotherapy for node-positive breast cancer?** *Int. J. Radiation Oncology Biol. Phys.* Vol 95 issue 3 1st June 2005 pp 386-391.
29. Zolta n varga et al, **Role of systemic therapy in the development of lung sequelae after conformal radiotherapy in breast cancer patients,** *Int. J. Radiation Oncology Biol. Phys.*, Vol. 80, No. 4, pp. 1109–1116, 2011.
30. Marie overguard et al, **Is the benefit of postmastectomy irradiation limited to patients with four or more positive nodes, as recommended in international consensus reports? A subgroup analysis of the DBCG 82 b&c randomized trials,** *Radiotherapy and Oncology* 82 (2007) 247–253.
31. Sung Ho Moon et al, **Radiation-induced Pulmonary Toxicity following Adjuvant Radiotherapy for Breast Cancer,** 대한방사선종양학회지 2007;25(2):109~117.
32. Pehr A.R.M Lind et al, **Abnormalities by pulmonary regions studied with computer tomography following local-regional radiotherapy for breast cancer,** *Int. J. Radiation Oncology, Biol. Phys.*, Vol. 43, No 3, pp 489-496, 1999.
33. Katrien erven et al, **Changes in pulmonary function up to 10 years after loco regional breast irradiation,** *Int. J. Radiation Oncology Biol. Phys.*, Vol. 82, No. 2, pp. 701–707, 2012.
34. Randi Vagane et al, **Radiological and functional assessment of radiation-induced pulmonary damage following breast irradiation** *Acta Oncologica*, 47:2, 248-254.
35. Ulla Blom Goldman et al, **Long-term functional and radiological pulmonary changes after radiation therapy for breast cancer,** *Acta Oncologica*, 53:10, 1373-1379.



- 36.Sylvia Verbanck et al, **Mild Lung Restriction in Breast Cancer Patients After Hypofractionated and Conventional Radiation Therapy: A 3-Year Follow-Up**, *Int J Radiation Oncol Biol Phys*, Vol. 95, No. 3, pp. 937e945, 2016.
- 37.Pulmonary Changes After Radiotherapy for Conservative Treatment of Breast Cancer: A Prospective Study *IJROBP* 2008 ;70:1460-1467.
- 38.A. E. Nordenskjöld et al, No clear effect of postoperative radiotherapy on survival of breast cancer patients with one to three positive nodes: a population-based study, *Annals of Oncology* 26: 1149–1154, 2015.
- 39.Thomas A. Buchholz et al, Lung Carcinoma Development after Radiotherapy for Breast Carcinoma *CANCER* October 1, 2003 / Volume 98 / Number 7.
- 40.Bagher Farhood ,et al Skin Reaction in Radiation Therapy for Breast Cancer, *Iranian Journal of Medical Physics* Vol. 11, No. 4, Autumn 2014, 316-321.
- 41.Madu C, Quint D, Normolle D, et al: Definition of the supraclavicular and infraclavicular nodes: Implications for three-dimensional CT-based conformal radiation therapy. *Radiology* 221:333-339, 2001.
- 42.L. Cozzi et al. Clinical experience in breast irradiation with intensity modulated photon beams, *Acta Oncologica*, 2005; 44: 467/474.
- 43.Alessio G. Morganti et al, Forward planned intensity modulated radiotherapy (IMRT) for whole breast postoperative radiotherapy. Is it useful? When?, *Journal of Applied Clinical Medical Physics*, Vol 12, No 2 (2011).
- 44.Beata Sas-Korczyn´ ska et al, Comparison between intensity modulated radiotherapy (IMRT) and 3D tangential beams technique used in patients with early-stage breast cancer who received breast-conserving therapy, *reports of practical oncology and radiotherapy* 1 5 ( 2 0 1 0 ) 79–86.

45. Indra J. Das et al, Correlation of 2D parameters to lung and heart dose-volume in radiation treatment of breast cancer, *Acta Oncologica*, 52:1, 178-183.
46. Abram Recht et al, **Postmastectomy Radiotherapy: Guidelines of the American Society of Clinical Oncology**, *Journal of Clinical Oncology*, Vol 19, No 5 (March 1), 2001: pp 1539-1569.
47. Abram Recht et al, **Postmastectomy Radiotherapy: An American Society of Clinical Oncology, American Society for Radiation Oncology, and Society of Surgical Oncology Focused Guideline Update**, *J Clin Oncol* 34. © 2016 by American Society of Clinical Oncology.
48. Tse-kuan Yu et al, **Clinically relevant pneumonitis after sequential paclitaxel-based chemotherapy and radiotherapy in breast cancer patients** *Journal of the national cancer institute*, vol.96, no 22, nov 17, 2004
49. Zoltan varga et al, **Role of systemic therapy in the development of lung sequelae after conformal radiotherapy in breast cancer patients**, *IJROBP Vol 80, no 4, pp.1109-1116,2011*.
50. **Concurrent or sequential adjuvant letrozole and radiotherapy after conservative surgery for early stage breast cancer (CO-HO-RT)** *Lancet oncol* 2010;11 (3):258-265
51. Stefan Rosfors et al, **ROC curves and evaluation of radiation-induced pulmonary toxicity in breast cancer**, *Int. J. Radiation Oncology Biol. Phys.*, Vol. 64, No. 3, pp. 765–770, 2006.
52. Hiram A. Gay et al, **A free program for calculating EUD- based NTCP and TCP in external beam radiotherapy**, *Physica Medica* (2007) 23, 115-125.

## APENDIX I

### DATA CAPTURE FORM

S.No	Parameter/Variable
1	ID
2	Age
3	Height
4	Weight
5	Body mass index
6	Smoking/exposure to smoking
7	Comorbid illness
8	Previous pulmonary diseases
9	Clinical stage
10	Side of treatment
11	Post-Operative (PO) HPE
12	Pathological stage
13	Sequence of treatment
14	Type of chemotherapy
15	Hormonal therapy
16	Chest X rays- prior to treatment, prior to radiation 1 year post treatment
17	Modified WHO score for RPT
18	Lung related morbidity and admissions during Chemotherapy, Radiotherapy, Follow up.
19	Apical lung distance
20	Lung length
21	Central lung distance
22	Superior and Inferior lung distance
23	Average lung distance
24	Maximum lung distance
25	SCL Fields
26	Total Volume of lung on the treated side
27	Total volume of lung contralateral side
28	Relative lung volumes V5,V10,V15,V20,V25,V30,V35,V40
29	Absolute lung volumes V5cc,V10cc,V15cc,V20cc,V25cc,V30cc,V35cc,V40cc
30	Lung doses D25, Minimum lung dose, Maximum Lung dose, Mean Lung dose
31	Relative lung volumes without SCL Field V5,V10,V15,V20,V25,V30,V35,V40
32	Absolute lung volumes without SCL Field V5cc,V10cc,V15cc,V20cc,V25cc,V30cc,V35cc,V40cc
33	Lung doses without SCL Field , D25,Minimum lung dose, Maximum Lung dose, Mean Lung dose
34	NTCP for Lung with and without SCL

S no	yr	Age	Ht	HT_M	HT2	Wt	BMI	smoki	hust	DM	Htr	BA	PTB	T	N	c STAGE	CSTAGE	side	SIDECODE	HIST	Grade	Pt	Pn	p St: LI	L1_ LII	LII_ LIII
1	15	40	142	1.42	2.0164	65	32.23566753	2	2	2	2	2	2	2	1	1 IIA	2A	R	1 IDC	III		2		2 IIAA	4 13	0 0 0
2	15	52	155	1.55	2.4025	77	32.04994797	2	2	1	1	2	2	2	2	2 IIAA	3A	R	1 IDC	III		1		2 IIAA	6 15	0 0 0
3	15	46	148	1.48	2.1904	63	28.76186998	2	2	2	2	2	2	2	2	1 IIB	2B	R	1 IDC	III		2		1 IIB	2 17	0 1 0
4	14	43	150	1.5	2.25	62	27.55555556	2	1	2	1	2	2	2	2	1 IIB	2B	L	2 IDC	III		3		0 IIB	0 16	0 1 0
5	15	45	144	1.44	2.0736	53	25.55941358	2	2	2	2	1	2	2	2	1 IIB	2B	I	2 IDC	III		1		0 IA		
6	15	51	157	1.57	2.4649	83	33.67276563	2	2	2	2	1	2	2	2	1 IIB	2B	R	1 IDC	II-III		2(IV		1 IIB	3 25	0 0 0
7	14	35	162	1.62	2.6244	78	29.7210791	2	1	1	2	2	2	2	2	1 IIB	2B	L	2 IDC	High grade		2		2 IIAA	8 12	1 7 0
8	15	50	152	1.52	2.3104	84	36.35734072	2	2	2	2	2	2	2 4b		1 IIBB	3B	R	1 IDC	III		2		1 IIB	2 22	0 4 0
9	15	56	140	1.4	1.96	61	31.12244898	2	1	2	2	2	2	2	2	2 IIAA	3A	R	1 IDC	III		2		1 IIB	2 9	0 2 0
10	15	68	144	1.44	2.0736	45	21.70138889	2	2	2	1	2	2	2	2	2 IIAA	3A	R	1 IDC	II		2		2 IIAA	6 12	1 3 0
11	15	48	150	1.5	2.25	57	25.33333333	2	2	1	1	2	2	2	3	1 IIAA	3A	R	1 Large cell	High grade		3		1 IIAA	1 14	0 5 0
12	15	62	165	1.65	2.7225	71	26.07897153	1	2	2	1	2	2	2	2	1 IIB	2B	L	2 IDC	III		2		1 IIB	1 13	0 1 0
13	15	60	147	1.47	2.1609	54	24.98958767	1	1	2	2	2	2	2 4b		2 IIBB	3B	R	1 IDC	III		2		2 IIAA	6 15	0 3 0
14	15	60	160	1.6	2.56	88	34.375	1	1	2	1	2	2	2	3	2 IIAA	3A	L	2 IDC	III		2		1 IIB	1 15	0 3 0
15	15	38	154	1.54	2.3716	72	30.35925114	2	2	2	2	2	2	2	2	1 IIB	2B	R	1 IDC	II		2		1 IIB	1 25	0 5 0
16	15	46	155	1.55	2.4025	80	33.29864724	2	2	2	2	2	2	2	3	1 IIAA	3A	L	2 IDC 40% I	II-III		3		0 IIB	0 10	0 4 0
17	15	42	157	1.57	2.4649	86	34.88985354	2	2	2	2	2	2	2	3	1 IIAA	3A	R	1 ILC	II		2		1 IIB	1 16	2 5 0
18	14	32	148	1.48	2.1904	42	19.17457999	1	2	2	2	2	2	2 (m)		1 IIB	2B	R	1 IDC	III		3		1 IIAA	3 16	0 6 0
19	15	61	152	1.52	2.3104	53	22.93975069	2	2	1	2	2	2	2	2	1 IIB	2B	L	2 IDC	III		2		2 IIAA	5 15	0 1 0
20	15	51	142	1.42	2.0164	67	33.22753422	2	1	1	1	2	2	2	2	2 IIAA	3A	L	2 IDC	III		2		2 IIAA	4 10	0 1 0
21	15	51	148	1.48	2.1904	52	23.73995617	2	1	2	2	1	2	2	3	2 IIAA	3A	L	2 IDC	III		MIC		1 IIA	1 15	0 0 0
22	15	45	162	1.62	2.6244	66	25.1486054	2		1	1	2	2	2	2	2 IIAA	3A	R	1 IDC	III		1		3 IIIC	9 10	0 0 1
23	15	53	152	1.52	2.3104	81	35.05886427	2	2	2	1	2	2	2	1	1 IIA	2A	R	1 IDC	III		1		1 IIA	3 20	0 0 0
24	15	51	157	1.57	2.4649	65	26.37023814	2	2	2	2	2	2	2 MASTECTOMY OS			L	2 IDC	III							
25	15	55	150	1.5	2.25	64	28.44444444	2	2	1	2	2	2	2	1	0 IA	1A	R	1 IDC	III		3		2 IIAA	4 12	0 2 0
26	15	47	151	1.51	2.2801	50	21.92886277	2	1	2	2	2	2	2	3	2 IIAA	3A	R	1 IDC	III		2		0 IIA	0 14	0 1 0
27	15	51	153	1.53	2.3409	64	27.339912	2	2	1	2	2	2	2	2	1 IIB	2B	L	2 IDC	III		2		3 IIIC	8 25	
28	15	55	155	1.55	2.4025	82	34.13111342	2	2	2	2	1	2	2	2	2 IIAA	3A	L	2 IDC	III		2		2 IIAA	4 14	0 3 0
29	15	50	167	1.67	2.7889	85	30.47796622	2	2	1	1	1	2	2	1	1 IIA	2A	R	1 IDC+ILC	III		1		2 IIAA	6 20	1 2 0
30	15	35	157	1.57	2.4649	68	27.58732606	2	1	2	2	2	2	2	2	1 IIB	2B	L	2 IDC	I		1		1 IIA	1 17	0 1 0
31	14	47	154	1.54	2.3716	66	27.82931354	2	1	1	2	2	2	2	2	1 IIB	2B	R	1 IDC	II-III		2		1 IIB	2 16	0 1 0
32	15	24	155	1.55	2.4025	56	23.30905307	2	2	2	2	2	2	2	3	1 IIAA	3A	L	2 IPC	II		2		1 IIB	1 11	0 1 0
33	15	45		0	0		#DIV/0!	2	1	2	1	2	2	2	2	2 IIAA	3A	L	2 IDC+ILC	II		1		2 IIAA	7 13	0 1 1
34	15	43	147	1.47	2.1609	50	23.1385071	2	2	1	2	2	2	2	1	1 IIA	2A	R	1 IDC	III		2 3a		IIIC	7 17	2 2 1
35	15	54	159	1.59	2.5281	73	28.87544005	2	2	1	2	2	2	2	2	1 IIB	2B	L	2 ILC	II		X		2 III	5 10	2 2 0
36	15	51	151	1.51	2.2801	53	23.24459454	2	2	1	2	2	2	2	2	2 IIAA	3A	L	2 IDC	III		1		2 IIAA	5 8	1 3 0
37	15	41	155	1.55	2.4025	52	21.64412071	2	2	2	2	2	2	2 MASTECTOMY OS			R	1 IDC	I-II			1		1 IIA		
38	15	33	167	1.67	2.7889	65	23.30668005	2	2	2	2	2	2	2	2	1 IIB	2B	R	1 IDC	III		2 3a		IIIC	11 12	8 9 5
39	15	50	149	1.49	2.2201	77	34.68312238	2	2	1	1	2	2	2 ?3		1 IIAA	3A	R	1 IDC	III		0		0 0	0 13	0 4 0
40	15	51	156	1.56	2.4336	60	24.65483235	2	2	1	2	2	2	2	1		2A	L	2 IDC	III		1		1 IIA	2 6	0 1 0
41	14	40	150	1.5	2.25	54	24	2	2	2	2	2	2	2	2	2 IIAA	3A	L	2 IDC	III		2(IV		2 IIAA	9 19	0 0 0
42	15	26	150	1.5	2.25	45	20	2	2	2	2	2	2	2	2	0 IIA	2A	L	2 IDC	II-III		2		3 IIIC	13 20	7 7 0
43	15	58	153	1.53	2.3409	72	30.757401	2	2	1	1	2	2	2	2	1 IIB	2B	L	2 ILC	III		2		3 IIIC	9 14	1 2 1
44	15	48	155	1.55	2.4025	52	21.64412071	2	2	2	2	2	2	2 MRM OS			R	1 IMC	III					2 III		
45	15	52	149	1.49	2.2201	62	27.92666997	2	2	2	2	2	2	2	0	2 III	3b	R	1 POORLY DIFFERENTI	X				0	0 17	0 2 0
46	14	50	152	1.52	2.3104	65	28.13365651	2	2	2	2	2	2	2	2	2 IIAA	3A	L	2 IDC	III		2		3 IIIC	8 10	2 2 1
47	15	49	153	1.53	2.3409	86	36.73800675	2	1	1	1	2	2	2 4b		2 IIBB	3B	L	2 IDC	II		1		1 IIA	2 5	1 1 0
48	14	42	147	1.47	2.1609	60	27.76620852	2	2	2	2	2	2	2	2	1 IIB	2B	L	2 IMC (duct	High grade mic				0 IA	0 21	0 4 0
49	15	51	154	1.54	2.3716	61	25.72103221	2	2	1	2	2	2	2	1	0 IA	1A	R	1 IDC	III		2		1 IIB	1 10	0 8 0
50	15	43	144	1.44	2.0736	46	22.18364198	2	1	2	2	2	2	2	2	1 IIB	2B	R	1 DCIS WIT	HG		1b		1 IIA	1 15	0 0 0

S no	yr	Age	Ht	HT_M	HT2	Wt	BMI	smoki	husi	DM	Htr	BA	PTB	T	N	c STAGE	CSTAGE	side	SIDECODE	HIST	Grade	Pt	Pn	p St: LI	L1_LII	LII_LIII
51	15	43	152	1.52	2.3104	65	28.13365651	2	2	1	2	1		2	2	2 IIIA	3A	R	1 IDC	III		2		1 IIB	2 20	0 3 0
52	15	58	142	1.42	2.0164	51	0	2	2	2	2	2		2	2	0 IIA	2A	R	1 IDC	III		2		3	10 10	2 2 0
53	15	65	145	1.45	2.1025	57	27.11058264	2	2	1	2	2		2	2	2 IIIA	3A	R	1 IDC	III		1		1 IIA	1 15	0 7 0
54	15	57	153	1.53	2.3409	80	34.17489	2	2	1	2	1		2	2	2 IIIA	3A	L	2 IDC	III		2		2 IIIA	5 13	0 2 0
55	15	35	156	1.56	2.4336	48	19.72386588	2	2	2	2	2		2	3	1 IIIA	3A	R	1 IDC	II		3		1 IIIA	2 14	0 4 0
56	15	51	150	1.5	2.25	72	32	2	2	1	2	2		2	2	1 IIB	2B	L	2 IDC+ILC	III		2		1 IIB	1 16	0 0 0
57	15	47	163	1.63	2.6569	56	21.07719523	2	2	1	2	2		2	2	1 IIB	2B	R	1 IDC	III		3		0 IIB	0 10	0 2 0
58	15	66	151	1.51	2.2801	62	27.19178983	2	2	2	2	2		1	3	2 IIIA	3A	L	2 IDC	III		2		1 IIB	2 4	0 2 0
59	15	66	151	1.51	2.2801	62	27.19178983	2	2	1	1	2		2	2	0 IIA	2A	R	1 IDC	III		2		1 IIB	1 17	0 0 0
60	15	60	156	1.56	2.4336	80	32.8731098	2	2	1	2	2		2	2	2 IIIA	3A	L	2 IDC	III		2		3 IIIC	7 18	0 1 0
61	15	66	151	1.51	2.2801	62	27.19178983	2	2	1	1	2		2	2	0 IIA	2A	R	1 IDC	III		1		1 IIA	1 17	0 0 0
62	15	60	150	1.5	2.25	90	40	2	2	2	1	2		2	2	1 IIB	2B	L	2 IDC	II-III		X/1		2 IIIA	3 7	1 2 0
63	15	52	159	1.59	2.5281	76	30.06210197	2	2	1	1	2		2	2	1 IIB	2B	R	1 IDC	III		2		1 IIB	3 14	0 3 0
64	15	50	160	1.6	2.56	55	21.484375	2	2	2	2	2		2	2	2 IIIA	3A	L	2 IDC+NEF	III		2		1 IIB	2 13	0 5 0
65	14	45	151	1.51	2.2801	62	27.19178983	2	1	1	2	2		2	2	1 IIB	2B	L	2 IDC	III		2		1 IIB	1 15	0 2 0
66	15	32	160	1.6	2.56	53	20.703125	2	2	2	2	2		2 2(m)		1 IIB	2B	R	1 IDC	III		2(m		1 IIB	2 9	0 1 0
67	15	36	157	1.57	2.4649	44	17.85062274	2	2	2	2	2		2	2	1 IIB	2B	R	1 IDC			1		2 IIIA	5 21	0 0 0
68	15	45	152	1.52	2.3104	64	27.70083102	2	1	2	2	2		2	2	1 IIB	2B	R	1 IDC	III		2		1 IIB	2 17	0 4 0
69	15	49	163	1.63	2.6569	79	29.73390041	2	2	2	1	2		2 4b		1 IIIB	3B	L	2 IDC	III		0		0 0	0 24	0 6 0
70	15	50	154	1.54	2.3716	39	16.44459437	2	2	2	2	2		2		2 IIIA	2A	R	1 IDC	III		1(m		1 IIA	1 6	0 4 0
71	15	43	160	1.6	2.56	48	18.75	1	1	2	2	2		2	2	2 IIIA	3A	R	1 IDC	III		1		1 IIA	1 17	1 2 0
72	15	60	146	1.46	2.1316	46	21.58003378	2	2	2	2	2		2	2	1 IIB	2B	L	2 IDC	II		2		1 IIB	1 18	0 5 0
73	14	63	149	1.49	2.2201	54	24.32322868	2	2	2	2	2		1	2	1 IIB	2B	L	2 IDC	III		2		3 IIIC	9 19	1 2 0
74	14	39	157	1.57	2.4649	65	26.37023814	2	2	2	2	2		2	2	2 IIIA	3A	L	2 IDC	III		0		1 IIA	3 7	0 1 0
75	14	60	154	1.54	2.3716	38	16.0229381	2	2	2	2	2		2	2	1 IIB	2B	L	2 IDC	III		2		1 IIB	3 10	0 3 0
76	15	65	157	1.57	2.4649	54	21.90758246	1	2	2	2	2		2	2	1 IIB	2B	L	2 IDC	III		3		1 IIIA	1 13	0 2 0
77	14	42	147	1.47	2.1609	74	34.24499051	2	2	2	2	2		2	1	1 IIA	2A	LEFT	2 IDC			2		1 IIB	3 23	0 5 0
78	14	56	158	1.58	2.4964	63	25.23634033	2	2	1	1	2		2	2	1 IIB	2B	LEFT	2 IDC			2 3a		III C	0 14	1 3 2
79	14	63	153	1.53	2.3409	55	23.49523687	2	2	2	2	2		2	2	2 III A	3A	RIGHT	1 IDC			1		1 IIA	3 20	0 1 0
80	15	68	153	1.53	2.3409	63	26.91272587	2	2	2	1	2		2	3	2 III A	3A	LEFT	2 IDC			2		2 III A	7 9	0 0 0
81	14	33	160	1.6	2.56	79	30.859375	2	2	2	2	2		2 4b		1 IIIB	3B	R	1 IDC	III		2		0 IIA	0 20	0 2 0
82	14	65	155	1.55	2.4025	63	26.2226847	1	2	2	2	2		2	2	1 IIB	2B	RIGHT	1 IDC			4a		2 III B	4 16	0 3 0
83	14	54	146	1.46	2.1316	75	35.18483768	2	2	2	1	2		2	3	1 III A	3A	RIGHT	1 IDC			2m 1a		II B	2 23	0 1 0
84	14	60	156	1.56	2.4336	53	21.77843524	2	2	1	1	2		2	3	2 III A	3A	LEFT	2 IDC			2 1a		II B	2 12	0 2 0
85	15	53	150	1.5	2.25	68	30.22222222	2	2	2	2	2		2 4B		1 III B	3B	RIGHT	1 IDC			2		0 IIA	0 12	0 3 0
86	15	43	159	1.59	2.5281	80	31.64431787	2	2	2	2	2		2 4b		2 III B	3B	RIGHT	1 medullary features			1		0 I A	0 21	0 0 0
87	15	54	156	1.56	2.4336	64	26.29848784	2	2	2	1	2		2	3	2 III A	3A	RIGHT	1 IDC			2		1 IIB	1 8	0 3 0
88	14	52	150	1.5	2.25	51	22.66666667	2	2	2	2	2		2	2	1 IIB	2B	LEFT	2 IDC			2 3a		III C	7 25	3 4 0
89	14	34	155	1.55	2.4025	65	27.05515088	2	2	2	2	2		2 4b		2 III B	3B	LEFT	2 IDC			2 3a		III C	7 15	4 4 1
90	15	37	164	1.64	2.6896	75	27.88518739	2	2	2	2	2		2 3/4b		1 III B	3B	LEFT	2 IDC			2		2 III A	4 16	0 0 0
91	15	37	155	1.55	2.4025	47	19.56295525	2	2	2	2	2		2	2	0 IIA	2A	RIGHT	1 IMC			1(Iv 3a		III C	2 20	2 5 2
92	15	40	150	1.5	2.25	67	29.77777778	2	2	2	2	2		2	2	1 IIB	2B	LEFT	2 IDC			2		1 IIB	3 23	0 6 0
93	15	57	163	1.63	2.6569	75	28.22838647	2	2	2	2	2		2	2	1 IIB	2B	RIGHT	1 IDC			1		2 III A	5 17	0 3 0
94	15	51	159	1.59	2.5281	68	26.89767019	1	1	1	1	2		2	2	1 IIB	2B	LEFT	2 IDC			2		1 IIB	1 13	0 2 0
95	14	43	160	1.6	2.56	74	28.90625	2	2	2	2	2		2	2	1 IIB	2B	LEFT	2 IDC			2 2a		III A	5 6	0 3 0
96	15	31	150	1.5	2.25	73	32.44444444	2	2	2	2	2		2	2	1 IIB	2B	LEFT	2 IDC			2		1 IIB	3 12	0 2 0
97	15	48	154	1.54	2.3716	63	26.56434475	2	2	1	1	2		2	2	2 III A	3A	LEFT	2 Mucinous carcinoma			2		1 IIB	2 13	0 3 0
98	14	67	152	1.52	2.3104	60	25.96952909	1	1	2	2	2		2	3	2 III A	3A	RIGHT	1 IDC			2		1 IIB	2 12	0 3 0
99	15	66	153	1.53	2.3409	51	21.78649237	2	2	2	2	2		2	2	1 IIB	2B	RIGHT	1 IDC			2		1 IIB	1 12	0 2 0
100	14	71	154	1.54	2.3716	41	17.2879069	1	1	2	1	2		2	2	0 IIA	2A	LEFT	2 IDC			2 1a		II B	0 0	0 0 0
101	14	46	143	1.43	2.0449	50	24.4510734	2	2	2	2	2		2	3	2 III A	3A	LEFT	2 IDC			2		0 IIA	0 11	0 1 0
102	14	50	154	1.54	2.3716	70	29.51593861	2	1	2	2	2		2 4b		1 III B	3B	RIGHT	1 IDC			0		0 0	0 22	0 8 0

S no	yr	Age	Ht	HT_M	HT2	Wt	BMI	smoki	husi	DM	Htr	BA	PTB	T	N	c STAGE	CSTAGE	side	SIDECODE	HIST	Grade	Pt	Pn	p St: LI	L1_LII	LII_LIII	
103	14	31	148	1.48	2.1904	72	32.87070855	2	2	2	2	2	2	2	3	1 III A	3A	LEFT	2 IDC			3 3a		III C	9 14	2 3	2
104	15	49	185	1.85	3.4225	66	19.28414901	2	2	2	2	2	2	2 3/4B		1 IIIB	3B	RIGHT	1 IDC			2(IV		1 II B	1 15	1 5	0
105	15	57	143	1.43	2.0449	55	26.89618074	2	2	1	1	2	2	2	3	1 III A	3A	LEFT	2 IDC			2		0 II A	0 7	0 1	0
106	15	58	152	1.52	2.3104	56	24.23822715	2	2	1	2	2	2	2	2	1 II B	2B	RIGHT	1 IDC			2		1 II B	2 12	0 1	0
107	14	51	149	1.49	2.2201	64	28.82753029	2	2	2	2	2	2	2	2	1 II B	2B	LEFT	2 IDC			3a		III C	15 20	0 1	0
108	14	67	150	1.5	2.25	82	36.44444444	1	1	2	2	2	2	2	2	2 III A	3A	LEFT	2 IDC			2 3a		III C	1 2	0 2	1
109	14	55	155	1.55	2.4025	60	24.97398543	2	2	2	2	2	2	2	2	1 II B	2B	LEFT	2 IDC			3		1 III A	2 12	0 0	0
110	14	31	149	1.49	2.2201	68	30.62925093	2	1	2	2	2	2	2 4B(M)		2 III B	3B	RIGHT	1 IDC			1		1 II A	2 9	0 1	0
111	14	53	163	1.63	2.6569	63	23.71184463	1	1	1	1	2	2	2	2	2 III A	3A	LEFT	2 IDC+NEF			2 3a		III C	9 9	1 1	2
112	14	45	150	1.5	2.25	65	28.88888889	2	2	1	1	2	2	2	2	0 II A	2A	RIGHT	1 IDC			2		1 II B	2 13	0 3	0
113	14	33	155	1.55	2.4025	47	19.56295525	2	2	2	2	2	2	2 EX		1	2A	LEFT	2 metaplastic carcinon			2		0 II A	0 20	0 0	0
114	15	61	153	1.53	2.3409	50	21.35930625	2	2	2	2	2	2	2	3	2 III A	3A	LEFT	2 IDC			2		2 III A	7 17	0 2	0
115	14	44	153	1.53	2.3409	56	23.922423	2	2	2	2	2	2	2	2	1 II B	2B	LEFT	2 IDC			2 2a		III A	4 10	0 0	0
116	15	43	157	1.57	2.4649	63	25.5588462	2	2	2	2	2	2	2	2	1 II B	2B	RIGHT	1 IDC			2(IV		1 II B	3 9	0 2	0
117	14	54	158	1.58	2.4964	68	27.23922448	2	2	1	1	2	2	2 EX		2	3A	RIGHT	1 IDC			x 2a		III A	4 16	0 1	0
118	14	61	158	1.58	2.4964	55	22.03172568	1	1	1	1	2	2	2 4b		1 III B	3B	RIGHT	1 IDC			1		0 I A	0 8	0 0	0
119	14	50	152	1.52	2.3104	55	23.80540166	2	2	2	2	2	2	2	3	2 IIIA	3A	R	1 IDC	III		3 3a		IIIA	21 21	2 2	4
120	15	53	160	1.6	2.56	78	30.46875	2	2	2	2	2	2	2	3	1 III A	3A	LEFT	2 IDC			1(IV		2 III A	8 15	0 1	0
121	14	70	160	1.6	2.56	60	23.4375	2	2	1	1	2	2	2	3	1 III A	3A	RIGHT	1 IDC			3 1a		III A	3 13	0 14	0
122	14	51	150	1.5	2.25	71	31.55555556	2	2	1	1	2	2	2	3	1 III A	3A	LEFT	2 IDC			3 1a		III A			
123	15	48	155	1.55	2.4025	64	26.63891779	2	2	2	1	2	2	2 4b		1 III B	3B	LEFT	2 IDC			2		2 III A	7 14	0 1	0
124	14	45	157	1.57	2.4649	64	25.96454217	1	2	1	1	2	2	2	2	1 II B	2B	RIGHT	1 IDC			3 3a		III C	5 12	3 5	1
125	14	67	160	1.6	2.56	50	19.53125	2	2	1	1	2	2	2	2	1 II B	2B	RIGHT	1 IDC			2		1 II B	1 15	0 0	0
126	14	56	148	1.48	2.1904	56	25.56610665	2	2	1	1	2	2	2	3	2 III A	3A	LEFT	2 IDC			2 3a		III C	6 13	0 1	1
127	14	50	150	1.5	2.25	50	22.22222222	2	2	2	1	2	2	2	2	2 III A	3A	LEFT	2 IDC			2 1a		II B	1 16	0 0	0
128	15	52	156	1.56	2.4336	51	20.9566075	1	1	1	1	2	2	2	3	2 III A	3A	LEFT	2 IDC			1		1 II A	1 17	0 1	0
129	14	61	140	1.4	1.96	44	22.44897959	1	2	1	1	2	2	2	3	1 III A	3A	LEFT	2 IDC			3 1a		III A	1 15	0 3	0
130	14	60	151	1.51	2.2801	70	30.70040788	2	1	2	1	2	2	2	2	1 II B	2B	RIGHT	1 IDC			2 3a		III C	5 13	0 0	1
131	14	52	151	1.51	2.2801	63	27.63036709	2	2	2	2	2	2	2	2	1 II B	2B	RIGHT	1 IDC			3(m		1 III A	3 18	0 4	0
132	15	43	152	1.52	2.3104	59	25.5367036	2	2	2	2	1	2	2	2	1 II B	2B	LEFT	2 IDC			2(IV		1 II B	2 10	0 1	0
133	15	45	150	1.5	2.25	66	29.33333333	2	2	2	2	2	2	2	3	1 III A	3A	LEFT	2 IDC			2 3a		III C	1 11	1 4	1
134	15	30	150	1.5	2.25	66	29.33333333	2	2	2	2	2	2	2	3	1 III A	3A	R	1 IDC			2 3a		III C	1 11	1 4	1
135	15	70	130	1.3	1.69	54	31.95266272	2	2	2	2	2	2	2 4b		2 IIIB	3B	R	1 IDC	III		2		3 IIIC	40 41	3	2
136	14	54	145	1.45	2.1025	54	25.68370987	2	2	2	1	2	2	2	2	1 II B	2B	LEFT	2 IDC			4a 3a		III C	4 13	1 2	1
137	15	46	150	1.5	2.25	53	23.55555556	2	2	2	2	2	2	2 2(M)		1 II B	2B	LEFT	2 IDC			2(IV		1 II B	2 13	0 4	0
138	14	61	152	1.52	2.3104	61	26.40235457	2	2	1	1	2	2	2	2	1 II B	2B	LEFT	2 IDC			2 1a		II B	2 12	0 1	0
139	15	50	148	1.48	2.1904	59	26.9357195	2	2	1	2	2	2	2	3	1 III A	3A	LEFT	2 IDC			1		0 I A	0 22	0 4	0
140	14	70	165	1.65	2.7225	58	21.30394858	1	1	1	1	2	2	2	3	1 III A	3A	RIGHT	1 IDC			1		0 I A	0 6	0 4	0
141	14	38	150	1.5	2.25	53	23.55555556	2	2	1	2	2	2	2	2	1 II B	2B	RIGHT	1 IDC			2		2 III A	4 17	1 1	0
142	14	32	167	1.67	2.7889	64	22.94811574	2	2	2	2	2	2	2	3	2 III A	3A	RIGHT	1 IDC			2		0 II A	0 13	0	0
143	15	55	143	1.43	2.0449	48	23.47303047	1	1	1	1	2	2	2	3	2 III A	3A	RIGHT	1 IDC			0		0 0	0 11	0 1	0
144	15	52	163	1.63	2.6569	73	27.47562949	1	1	1	2	2	2	2	3	2 III A	3A	LEFT	2 IDC			0		0 0	0 10	0 0	0
145	14	60	157	1.57	2.4649	79	32.04998174	1	1	1	2	2	2	2	2	2 III A	3A	LEFT	2 ILC+NEF			2		1 II B	1 11	0 2	0
146	14	32	158	1.58	2.4964	56	22.43230252	2	1	2	2	2	2	2 IS	X	0 0	0 0	RIGHT	1 IDC			2 1a		II B	1 19	0 3	0
147	14	50	155	1.55	2.4025	70	29.13631634	2	2	2	2	2	2	2	2	2 III A	3A	RIGHT	1 IDC			0 2a		III A	5 15	0 3	0
148	15	47	150	1.5	2.25	79	35.11111111	2	2	2	2	2	2	2	2	1 II B	2B	RIGHT	1 IDC+ILC+ADH			2		1 II B	3 12	0 1	0
149	14	49	155	1.55	2.4025	73	30.38501561	2	2	2	2	2	2	2	2	1 II B	2B	RIGHT	1 IDC			2 3a		III C	9 17	1 1	1
150	14	30	158	1.58	2.4964	50	20.02884153	1	2	1	1	2	2	2 1(M)		1 II A	2A	LEFT	2 IDC			1(IV 2a		III A	4 24	0 6	0
151	14	48	155	1.55	2.4025	75	31.21748179	2	2	2	2	2	2	2 EX		1	2B	LEFT	2 IDC			2 1a		II B	1 17	1 1	0
152	14	47	157	1.57	2.4649	49	19.8791026	2	1	1	2	2 IS		X		0 0	II A	RIGHT	1			1 1 2a		1	14 1	1 0	0

LIIL_TOT	TOT_PNS	LVI	PN	ER	PR	Her2	Ki	p Stage	PSTAGE	Final Stage	FINALSTA	TRT	TRT_TY	TYPE_CT	CT CO HT	PRE_R	PRERXCO	PRE_F	1 1YRC	Area_A	Shadow	SUM	ASD				
0	4	14	1	1NO	2	2	2	0	60	IIIA	3A	IIIA	3A	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	6	15	1	2	2	1	1	3		IIIA	3A	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	2	18	1	2	2	2	2	2	50	IIB	2B	IIB	2B	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	0	2	NAD	1	1	0	0.0	0	0+0+0
3	0	20	2	2	2	1	1	3	70	IIB	2B	IIB	2b	SX-6FEC-RT-HT	1	6FEC	2	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
	0	14	2	2	2	1	1	0	10	IA	1A	IA	2A	SX-6FE-RT-HT	1	6FEC	2	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
4	3	29	1	2	2	1	1	2	10	IIB	2B	IIB	2B	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1	0.5	1.5	1+0.5+0
3	9	12	1	1	2	1	1	3	80	IIIA	3A	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	2	26	2	1NO	2	1	1	3	40	IIB	2B	IIIB	3B	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
2	2	13	1	1NO	1	2	2	3	60	IIB	2B	IIB	2B	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
4	7	19	1	1NC	2	1	1	2	30	IIIA	3A	IIIA	3A	3CMF-SX-3CMF-RT-HT	2	6CMF	3	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
3	1	22	2	2	2	2	2	2	70	IIIA	3A	IIIA	3A	SX-6EP-RT	1	6EP	5	1	0	2	NAD	1	1	0	0.0	0	0+0+0
1	1	15	2	1	2	1	1	2	30	IIB	2B	IIB	2B	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	6	19	2	1	2	1	1	3	40	IIIA	3A	IIIB	3B	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	nad	1	nad	1	1	0	0.0	0	0+0+0
0	1	18	2	2	2	1	2	2	70	IIB	2B	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1	0.5	1.5	1+0.5+0
5	1	35	2	2	2	1	1	2	30	IIB	2B	IIB	2B	SX3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	0	14	2	2	2	1	1	3		IIB	2B	IIB	2B	SX-6FEC-RT-HT	1	6FEC	2	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	3	21	1	2	2	1	1	1	30	IIB	2B	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	3	22	2	2	2	1	1	3	60	IIIA	3A	IIIA	3A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	5	17	1	2	2	1	1	3	5	IIIA	3A	IIIA	3A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1	0.5	1.5	1+0.5+0
0	4	11	1	2	2	1	1	3	40	IIIA	3A	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	1	0.5	1.5	1+0.5+0
1	1	16	1	2	2	2	1	3	70	IIA	2A	IIIA	3A	3TE-SX-3TE-RT-HT	2	6TE	4	2	NAD	1	NAD	1	1	1	1.0	2	1+1+0
1	10	11	1	2	2	1	1	3	60	IIIC	3C	IIIC	3C	3TE-SX-3TE-RT-HT	2	6TE	4	2	0	2	NAD	1	1	0	0.0	0	0+0+0
0	3	20	2	2	2	2	2	3	60	IIA	2A	IIA	2A	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
	5	7	1	2	2	1	1	2	70			3A	3A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	4	14	1	NOD	2	1	2	2	40	IIIA	3A	IIIA	3A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	0	15	2	1TU	2	2	2	2		IIA	2A	IIIA	3A	3FEC-SX-3DOC-RT	2	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
	10	32	1	1NC	2	2	2	3	70	IIIC	3C	IIIC	3C	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
2	4	19	1	1TU	2	1	2	2	60	IIIA	3A	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
3	6	25	1	2	2	1	1	0	60	IIIA	3A	IIIA	3A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	1	19	2	2	2	1	1	0	10	IIA	2A	IIA	2A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
5	2	22	2	2	2	1	1	3	20	IIB	2B	IIB	2B	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	1	12	1	2	2	1	1	0	10	IIB	2B	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
14	8	18	2	1TU	2	1	2	2	60	IIIA	3A	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	10	20	1	1turr	1	1	1	2	40	IIIC	3C	IIIC	3C	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	7	12	1	2	2	1	1	0	20	III	3	III	3b	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1	1.0	2	1+1+0
0	6	11	1	1NO	2	2	2	3	50	IIIA	3A	IIIA	3A	2FEC-SX-1FEC-3DOC-RT	2	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
	1	15	2	1	2	1	1	0	20	IIA	2A	IIA	2A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
6	30	33	1	1tur	2	1	2	0	70	IIIC	3C	IIIC	3C	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	0	18	2	2	2	2	2	2	90		0 0	IIIA	3A	1DEF+2FEC-SX-3DOC-RT	2	1DEF+2FEC+3F	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	2	8	2	2	2	1	1	2	50	IIA	2A	IIA	2A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	9	20	1	2	2	1	1	2	40	IIIA	3B	IIIA	3A	SX-6FEC-RT-HT	1	6FEC	2	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	20	27	1	1TU	2	1	1	0	70	IIIC	3C	IIIC	3C	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
16	11	22	1	1TU	2	2	2	3	60	IIIC	3C	IIIC	3C	SX-3FEC-RT-3DOC	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
	6	10	2	2	2	2	2	3	40	III	3	III	3b	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
3	0	22	2	2	2	2	2	2	70			3b	3b	SX-6TE-RT	1	6TE	4	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	11	13	1	1TU	2	1	1	3	50	IIIC	3C	IIIC	3C	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	3	6	2	2	2	1	1	2	40	IIA	2A	IIIB	3B	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	0	26	2	2	2	1	2	2	80	IA	1A	IIB	2B	2FEC-SX-4FEC-RT-HT	2	6FEC	2	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
0	1	18	2	2	2	1	1	3	50	IIB	2B	IIB	2B	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
1	1	16	2	2	2	2	2	2	10	IIA	2A	IIA	2A	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	0	2	NAD	1	1	0	0.0	0	0+0+0

LIIL_TOT	TOT_PNS	LVI	PN	ER	PR	Her2	Ki	p Stage	PSTAGE	Final Stage	FINALSTA	TRT	TRT_TY	TYPE_CT	CT CO HT	PRE_R	PRERXCO	PRE_F	1	1YRC	Area_A	Shadow	SUM	ASD			
2	2	25	1	2	1	1	2	IIB	2B	IIB	2B	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1	0.5	1.5	1+0.5+0		
2	12	14	1	1NO	2	1	2	40 IIIC	3C	IIIC	3C	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0		
1	1	23	2	2	2	1	2	3	60 IIA	2A	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
2	5	17	2	TUM	2	1	2	3	70 IIIA	3A	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1	0.5	1.5	1+0.5+0	
3	2	22	2	2	2	1	1	0	40 IIIA	3A	IIIA	3A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
1	1	17	2	2	2	1	1	2	70 IIB	2B	IIB	2B	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1	1.0	2	1+1+0	
4	0	16	2	2	2	1	1	3	70 IIB	2B	IIB	2B	SX-6FEC-RT-HT	1	6FEC	2	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
1	2	7	1	2	2	1	1	2	70 IIB	2B	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
0	1	17	2	2	2	1	2	2	50 IIB	2B	IIB	2B	2FEC-SX-1FEC-3DOC-RT-H	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
0	7	19	1	2	2	1	1	2	60 IIIC	3C	IIIC	3C	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	0	2	NAD	1	1	0	0.0	0	0+0+0	
0	1	17	2	2	2	1	2	2	50 IIA	2A	IIA	2A	2FEC-SX-1FEC-3DOC-RT-H	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
1	4	10	1	1	TU	2	1	1	2	30 IIIA	3A	IIIA	3A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
2	3	19	1	2	2	1	1	3	50 IIB	2B	IIB	2B	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
1	2	19	2	2	2	1	1	2	40-50 IIB	2B	IIIA	3A	2FEC-SX-1FEC-3DOC-RT-H	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
6	1	23	2	2	2	2	2	3	60 IIB	2B	IIB	2B	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
0	2	10	2	2	2	1	1	3	60 IIB	2B	IIB	2B	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
0	5	21	2	2	2	1	1	2	15-20 IIIA	3A	IIIA	3A	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
6	2	27	1	2	2	2	2	3	70 IIB	2B	IIB	2B	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
0	0	30	2	2	2	1	2	2	60	0 0	IIIB	3B	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	2	0	2	NAD	1	1	0	0.0	0	0+0+0	
2	1	12	1	1	2	2	2	2	70 IIA	2A	IIA	2A	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	0	2	NAD	1	1	0	0.0	0	0+0+0	
4	2	23	1	2	2	1	2	3	60 IIA	2A	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
0	1	23	1	1	NC	2	2	1	2	30 IIB	2B	IIB	2B	SX-3FEC-3DOC-RT-HT	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0	0+0+0
2	10	23	2	2	2	2	2	3	IIIC	3C	IIIC	3C	SX-3FEC-3DOC-RT	1	3FEC+3DOC	1	1	right Op	3	Same i	3	1	0	0.0	0	0+0+0	
2	3	10	1	2	2	1	1	3	70 IIA	2A	IIIA	3A	3TE-SX-3TE-RT-HT	2	6TE	4	2	NAD	1	NAD	1	1	0	0.0	0	0+0+0	
5	3	18	1	1	2	1	2	3	70 IIB	2B	IIB	2B	SX-6CMF-RT-HT	1	6CMF	3	3	Pleural t	3	BVM, I	3	1	1	0.5	1.5	1+0.5+0	
3	1	18	2	1	TUI	2	2	2	3	80 IIIA	3A	IIIA	3A	SX-6CMF-RT-HT	1	6CMF	3	1	NAD	1	NAD	1	1	1	1.0	2	1+1+0
2	3	30	2	1	1	1	1	2	60 II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NA	2	NAD	1	1	0.0	0.0	0	0+0+0	
3	3	20	2	2	1	1	2	3	40 III C	3C	III C	3C	sx-3fec-3doc	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
2	3	23	2	1	1	1	2	3	II A	2A	II A	2A	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NA	2	NAD	1	1	0.0	0.0	0	0+0+0	
3	7	12	2	1	1	1	1	3	60 III A	3A	III A	3A	3FEC-SX-3DOC	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
0	0	22	2	2	2	1	1	10	60 IIA	2A	IIIB	3B	2FEC-SX-4FEC-RT-HT	2	6FEC	2	2	NAD	1	calcifie	3	1	0	0.0	0	0+0+0	
3	4	22	2	1	1	1	1	3	70 III B	3B	III B	3B	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1.0	0.5	2.5	1+0.5+1	
4	2	28	2	1	1	2	2	1	II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
0	2	14	2	1	2	1	1	3	80 II B	2B	IIIA	3A	3FEC-Sx-3Doc	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
2	0	17	1	1	1	1	2	3	70 II A	2A	IIIB	3B	3FEC-SX-3DOC	2	3FEC+3DOC	1	3	NA	2	NAD	1	1	0.0	0.0	0	0+0+0	
0	0	21	1	1	1	1	1	1	70 I A	1A	IIIB	3B	3TE-SX-3TE	2	6TE	4	2	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
2	1	13	2	1	1	1	1	2	50 II B	2B	IIIA	3A	3DC-SX-3DC	2	6DC	5	3	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
0	10	29	2	1	1	1	1		III C	3C	III C	3C	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NA	2	NAD	1	1	0.0	0.0	0	0+0+0	
2	12	21	2	2	1	1	1	1	40 III C	3C	III C	3C	3FEC-Sx-3Doc	2	3FEC+3DOC	1	2	NA	2	NAD	1	1	0.0	0.0	0	0+0+0	
0	4	16	2	1	1	1	1	3	30 III A	3A	IIIB	3B	3FEC-SX-3DOC	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
2	6	42	2	2	1	1	1	3	30 III C	3C	III C	3C	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
2	3	31	2	1	1	1	1	3	50 II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
0	5	20	2	1	1	1	1	3	40 III A	3A	III A	3A	SX-6TE	1	6TE	4	3	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
2	1	17	2	2	1	1	1	3	30 II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	1.0	0.5	1.5	1+0.5+0	
2	5	11	1	2	1	1	2	2	50 III A	3A	III A	3A	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
2	3	12	2	1	1	1	1	1	40 II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
1	2	17	1	1	1	1	1	3	45 II B	2B	IIIA	3A	3FEC-SX-3DOC	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	
3	2	18	1	1	1	1	1	3	40 II B	2B	IIIA	3A	3FEC-SX-3DOC	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1.0	0.5	1.5	1+0.5+0	
0	1	14	1	2	1	1	1	1	45 II B	2B	II B	2B	SX-CT-RT-HT	1	6FEC	2	3	NA	2	NAD	1	1	0.0	0.0	0	0+0+0	
4	0	4	2	1	1	1	1	3	10 II B	2B	II B	2B	SX-RT-HT	0	No	0	3	Tiny calc	3	static	3	1	1.0	0.5	1.5	1+0.5+0	
0	0	12	1	1	1	2	2	1	50 II A	2A	IIIA	3A	3FEC-SX-3DOC	2	3FEC+3DOC	1	1	NA	2	NAD	1	1	0.0	0.0	0	0+0+0	
0	0	30	1	1	1	1	1	3	80	0 0	IIIB	3B	3TE-SX-3TE	2	6TE	4	2	NAD	1	NAD	1	1	0.0	0.0	0	0+0+0	



LIIL_TOT	TOT_PNS	LVI	PN	ER	PR	Her2	Ki	p Stage	PSTAGE	Final Stage	FINALSTA	TRT	TRT_TYF	TYPE_CT	CT CO HT	PRE_R	PRERXCO	PRE_F	1	1YRC	Area_A	Shadow	SUM	ASD	
3	13	20	2	1	1	2	2	3	90 III C	3C	III C	3C	3TE-SX-3TE	2	6TE	4	1	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	2	21	2	1	1	1	1	3	2 II B	2B	IIIB	3B	3TE-SX-3TE	2	6TE	4	2	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	0	9	1	1	1	1	1	2	30 II A	2A	IIIA	3A	3FEC-SX-3DOC	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	2	14	2	1	1	1	2	3	40 II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
0	15	21	2	1	1	1	1	3	40 III C	3C	III C	3C	2TE-SX-2TE-RT-2TE-Hercej	2	6TE	4	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
13	2	17	2	1	1	1	1	3	70 III C	3C	III C	3C	3FEC-SX-3DOC	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1.0	0.5	1.5 1+0.5+0
2	2	14	1	1	1	1	1	3	60 III A	3A	III A	3A	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	2	11	2	1	1	2	2	2	2 II A	2A	IIIB	3B	3FEC-SX-3DOC	2	3FEC+3DOC	1	1	NA	2	NAD	1	1	0.0	0.0	0 0+0+0
2	12	12	2	1	1	1	2	2	20 III C	3C	III C	3C	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	1.0	0.5	1.5 1+0.5+0
4	2	20	2	1	2	1	1	3	50 II B	2B	II B	2B	3FEC-SX-TE+RT-HT	2	3FEC+3TE	5	2	NA	2	NAD	1	1	0.0	0.0	0 0+0+0
2	0	22	1	1	1	2	2	1	80 II A	2A	II A	2A	SX-6FEC	1	6FEC	2	1	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
4	7	23	2	1	1	1	2	3	40 III A	3A	III A	3A	3FEC-SX-3DOC	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
0	4	10	2	2	1	1	1	2	40 III A	3A	III A	3A	sx-3fec-3doc	1	3FEC+3DOC	1	2	NA	2	NAD	1	1	0.0	0.0	0 0+0+0
1	3	12	2	1	1	1	1	3	70 II B	2B	II B	2B	SX3FEC-3DOC	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
5	4	22	2	2	1	1	2	3	40 III A	3A	III A	3A	sx-3fec-3doc	1	3FEC+3DOC	1	3	NA	2	Fibrosi	3	1	0.0	0.0	0 0+0+0
0	0	8	1	1	1	1	2	3	70 I A	1A	IIIB	3B	3CMF-SX-3CMF	2	6CMF	3	3	NAD	1	NAD	1	1	1.0	0.5	1.5 1+0.5+0
4	28	28	1	1TU	1	1	2	1	40 IIIA	3A	IIIA	3A	3FEC-SX-3DOC-RT-HT	2	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0	0.0	0 0+0+0
0	8	16	2	1	1	2	2	3	40 III A	3A	IIIA	3A	3FEC-SX-3DOC	2	3FEC+3DOC	1	1	NA	2	NAD	1	1	0.0	0.0	0 0+0+0
3	3	30	2	1	1	2	2	2	70 III A	3A	III A	3A	SX-3FEC-3DOC	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
	1	21	1	1	1	2	2	1	III A	3A	III A	3A	SX-3FEC-3DOC	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	7	16	2	1	1	1	1	3	30 III A	3A	IIIB	3B	3FEC-SX-3DOC	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	9	18	2	2	1	1	1	3	80 III C	3C	III C	3C	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NA	2	NAD	1	1	2.0	1.0	3 2+1+0
2	1	17	1	1	1	2	1	1	30 II B	2B	II B	2B	SX-RT-HT	0	No	0	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
2	7	16	2	1	1	1	1	3	70 III C	3C	III C	3C	3fec-sx-3doc	2	3FEC+3DOC	1	3	NA	2	NAD	1	1	0.0	0.0	0 0+0+0
1	1	17	1	1	1	1	1	2	70 II B	2B	IIIA	3A	3FEC-SX-3DOC	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	1	19	1	2	2	2	2	3	II A	2A	II A	2A	SX-6FEC	1	6FEC	2	1	NAD	1	NAD	1	1	1.0	0.5	1.5 1+0.5+0
4	1	22	2	2	1	1	1	2	50 III A	3A	III A	3A	SX-3FEC-3PAC	1	3FEC+3PAC	1	3	NAD	1	NAD	1	1	2.0	1.0	4 2+1+1
2	6	15	2	2	1	1	1	3	30 III C	3C	III C	3C	sx-6fec	1	6FEC	2	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
2	3	24	1	2	1	1	2	2	60 III A	3A	III A	3A	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	2	14	2	1	1	1	1	2	30 II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
2	3	19	2	2	1	1	1	1	60 III C	3C	III C	3C	SX-6FEC	1	6FEC	2	2	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
2	3	19	2	2	1	1	1	1	60 III C	3C	III C	3C	SX-6FEC	1	6FEC	2	2				1	0.0	0.0	0 0+0+0	
3	45	47	1	1	2	2	2	3	IIIC	3C	IIIB	3B	3CMF-SX-3CMF-RT	2	6CMF	3	1	NAD	1	NAD	1	1	0	0.0	0 0+0+0
1	6	16	1	2	1	1	1	2	50 III C	3C	III C	3C	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	2	18	1	1	1	2	2	3	40 II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NA	2	NAD	1	1	0.0	0.0	0 0+0+0
1	2	14	2	1	1	1	1	3	40 II B	2B	II B	2B	sx-3fec-3doc	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
2	0	28	1	1	1	1	2	3	80 I A	1A	IIIA	3A	2FEC-SX-3DOC	2	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
0	0	10	1	1	1	2	2	3	70 I A	1A	IIIA	3A	3FEC-SX-3DOC	2	3FEC+3DOC	1	1	NAD	1	NAD	1	1	1.0	0.5	1.5 1+0.5+0
2	5	20	2	1	1	2	2	0	80 III A	3A	III A	3A	SX-3FEC-3DOC	1	3FEC+3DOC	1	1	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
5	0	18	1	1	1	2	2	3	80 II A	2A	IIIA	3A	3TE-SX-3TE	2	6TE	4	1	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	0	13	1	1	1	2	2	3	30	0 0	IIIA	3A	3TE-SX-3TE	2	6TE	4	1	NA	2	NAD	1	1	1.0	0.5	1.5 1+0.5+0
0	0	10	1	1	1	2	2	3	80	0 0	IIIA	3A	3FEC-SX-DOC	2	3FEC+3DOC	1	1	NA	2	NAD	1	1	1.0	0.5	1.5 1+0.5+0
2	1	15	1	1	1	1	1	3	70 II B	2B	IIIA	3A	3TE-SX-3TE	2	6TE	4	3	NAD	1	NAD	1	1	1.0	0.5	1.5 1+0.5+0
1	1	23	1	1	1	1	2	3	70 II B	2B	II B	2B	sx-3fec-3doc	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	5	19	1	1	1	1	2	2	50 III A	3A	III A	3A	3TE-SX-3TE	2	6TE	4	3	NA	2	NAD	1	1	0.0	0.0	0 0+0+0
1	3	14	2	1	1	1	1	0	20 II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
1	11	19	2	1	1	1	1	2	40 III C	3C	III C	3C	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
4	4	34	2	2	1	1	1	2	50 III A	3A	III A	3A	SX-3FEC-3DOC	1	3FEC+3DOC	1	2	NAD	1	NAD	1	1	1.0	0.5	1.5 1+0.5+0
1	2	19	2	1	2	1	2	3	20 II B	2B	II B	2B	SX-3FEC-3DOC	1	3FEC+3DOC	1	3	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0
2	15	1	1	1	1	1	3	30	SX-3F 2A	II A	2A	IDC	1	3FEC+3D	1	2	3.61	NAD	1	NAD	1	1	0.0	0.0	0 0+0+0

INCL	CT to R1	FU	mc	Apical	LL	CLD	ILD	SLD	AVG	MAX_LD	SCL	TRT	scltrt	VOL_Rx	Vol_opi	V5_SCL	V10_SCL	V15_SCL	V20_SCL	V25_SCL	V30_SCL	V35_SCL	V40_SCL	D25_SCL	V5CC_SCL	V10CC_SCL	V15CC_SCL	V20CC_SCL
1	5	21	1.92	10.5	3.08	2.88			2.54	2.83333	3.41	AP-PA	2	663	556	53.4	38.5	33.9	31.4	29.5	27.6	25.4	21.7	35.7	355	255	224	208
1	5	23	1.93	11.4	3.02	3.37			2.26	2.88333	3.4	AP-PA	2	942	840	47	32.2	26.9	24.4	22.7	21	19	15.1	18.4	441	303	253	230
1	6	22	1.39	11.5	2.57	2.54			1.51	2.20667	2.69	AP-PA	2	752	567	45.2	29.4	24.2	21.8	20.1	18.5	16.6	13.3	13.6	339	222	182	164
1	4	27	3.20	11.7	2.46	1.42			2.27	2.05	2.5	AP	1	643	736	41.8	30.7	27.4	25.5	23.9	22.3	19.7	14.1	21.7	269	197	176	164
1	5	19	2.38	11.7	2.51	2.9			1.92	2.44333	2.9	AP-PA	2	883	620	42.2	29.5	25.6	23.6	21.9	20.3	18.4	15	16.3	373	261	227	208
1	6	20	1.89	11.8	4.3	4.09			2.71	3.7	4.73	AP-PA	2	890	662	53.4	38.8	33.6	31.1	29.2	27.4	25.3	21.3	35.5	478	345	299	277
1	4	26	2.58	12.2	2.43	2.23			2.53	2.39667	2.95	AP-PA	2	764	924	47.9	33.3	29.4	27.3	25.7	23.9	21.7	17.1	27	365	255	224	209
1	4	19	1.44	12.3	3.23	2.5			2.39	2.70667	3.52	AP-PA	2	734	616	58.7	40.6	33.4	30	27.7	25.5	23.1	19.1	31.2	431	298	245	220
1	4	22	1.33	12.4	3.66	2.97			3.5	3.37667	3.96	AP-PA	2	823	553	53.9	39.4	34	31.2	29.3	27.4	25.2	21.4	35	442	325	280	258
1	4	21	1.93	12.6	3.14	3			2.38	2.84	3.33	AP-PA	2	850	557	55	39.2	33	29.9	27.9	26.1	24	20.5	32.9	469	335	280	255
1	4	23	2.40	12.7	3.1	2.94			2.58	2.87333	3.3	AP-PA	2	818	639	51.2	37.6	32.9	30.7	28.9	27.4	25.4	21.7	35.6	419	308	270	251
1	4	20	1.88	13.2	3.23	3.15			1.83	2.73667	3.6	AP-PA	2	887	1118	49.4	37.1	32.8	30.3	28.2	26.2	23.8	19.6	32.6	436	329	291	269
1	4	22	1.58	13.3	2.64	2.87			2.23	2.58	3.17	AP-PA	2	920	730	53	35.1	29.6	27.1	25.3	23.6	21.5	17.7	26	489	324	272	250
1	4	22	1.78	13.3	3.18	2.91			2.83	2.97333	3.31	AP-PA	2	912	1042	54.8	38.6	32	29.1	27	25.1	22.9	18.8	30.4	501	352	293	266
1	4	21	2.19	13.4	3.22	3			2.82	3.01333	3.29	AP-PA	2	894	688	52.8	37.3	31.6	29.1	27.3	25.7	23.9	20.8	32.1	472	333	283	260
1	3	23	2.16	13.4	3.39	3.37			2.3	3.02	3.53	AP-PA	2	993	1034	54	38.3	32.3	29.6	27.5	25.5	23	18.4	31.1	536	380	321	294
1	3	19	2.27	13.4	2.82	2.91			2.39	2.70667	3.11	AP-PA	2	1045	751	53.2	38.9	32.4	29.4	27.3	25.3	22.9	18.9	30.5	555	405	338	307
1	4	27	2.20	13.4	1.94	2.23			1.11	1.76	2.28	PA	1	871	671	49.1	34.8	29.7	27.1	25.1	23.1	20.9	16.4	25.2	432	304	259	236
1	5	20	2.52	13.6	2.66	2.24			2.75	2.55	2.94	AP-PA	2	713	897	52	38.7	33.7	30.7	28.2	25.7	22.9	17.8	31.4	372	275	240	218
1	5	26	2.38	13.7	2.52	2.59			2.29	2.46667	2.81	AP-PA	2	761	817	56.6	40.4	33.8	30.8	28.7	26.6	24.2	20	33.6	430	307	257	235
1	4	23	2.55	13.8	2.25	2.36			1.62	2.07667	2.29	AP-PA	2	563	763	52.6	37.8	32.8	30.2	28.3	26.3	24.1	20.8	33.1	297	213	185	170
1	4	22	2.51	13.8	3.18	3.03			2.52	2.91	3.76	AP-PA	2	1122	984	45.5	30	25.4	23.2	21.6	20.1	18.4	15.3	15.6	509	336	285	260
1	4	19	0.86	13.8	2.82	2.98			1.93	2.57667	3.18	AP-PA	2	1034	679	43.8	28.8	23.8	21.4	19.9	18.6	17.1	14.7	13.26	454	297	245	222
1	4	22	2.35	13.8	3.18	1.48			2.75	2.47	3.32	AP-PA	2	655	867	45.1	33.1	28.6	26.3	24.6	22.9	20.9	17.3	23.5	295	217	187	172
1	3	23	2.31	13.9	2.85	2.77			2.68	2.76667	3.39	AP-PA	2	894	691	56.3	39.6	33.6	30.6	28.5	26.7	24.5	21.4	34	504	354	300	274
1	4	21	2.66	13.9	2.77	2.93			2.8	2.83333	2.91	AP-PA	2	1129	929	53.3	37.8	32.2	29.7	27.8	26.1	24.1	19.8	32.7	602	427	364	335
1	4	25	1.90	13.9	2.91	2.62			2.14	2.55667	3.34	AP-PA	2	874	1043	48	30.4	25.4	23	21.4	19.8	18	15	15.6	417	266	222	201
1	5	22	1.93	13.9	2.51	2.96			2.05	2.50667	2.99	AP-PA	2	796	1149	53.5	39.3	34.2	31.6	29.6	27.7	25.4	21	35.7	425	313	272	251
1	5	21	1.43	14	2.17	2.89			2.59	2.55	2.98	AP-PA	2	950	802	45.6	30.8	26.3	23.9	22.1	20.4	18.3	14.9	17.5	434	293	250	227
1	3	18	2.04	14	2.67	2.39			2.8	2.62	3.4	AP-PA	2	619	849	46.9	36.1	32	29.8	28.1	26.4	24.3	20.3	33.7	290	224	198	185
1	4	29	2.24	14	2.86	2.54			2.86	2.75333	3.09	AP	1	867	620	54.9	37.9	32.9	30.5	28.5	26.7	24.4	20.4	33.8	471	329	286	264
1	4	19	2.06	14.1	2.83	3.29			2.56	2.89333	3.29	AP-PA	2	695	909	51	38.1	33.3	31	29.2	27.4	25.5	22.2	36.9	353	265	231	215
1	4	19	1.76	14.2	2.23	2.67			1.71	2.20333	2.78	AP-PA	2	740	852	50.4	33.9	28.6	26.2	24.5	23	21.2	18.2	23.6	371	251	216	194
1	4	20	1.62	14.2	2.74	2.86			2.43	2.67667	2.99	AP-PA	2	906	661	51.6	35.4	30.5	28.2	26.5	24.9	23.1	20.4	29.5	465	321	277	256
1	4	23	2.53	14.3	2.94	3.22			2.74	2.96667	3	AP-PA	2	769	908	51.9	39.1	34	31	28.3	25.6	23	19	31.2	397	301	261	239
1	4	22	1.00	14.3	2.96	2.9			2.71	2.85667	3.15	AP-PA	2	673	687	55.9	39.7	33.2	30.3	28.2	26.3	24.2	21.2	33.2	338	267	224	204
1	5	22	1.96	14.3	2.18	2.85			2.58	2.53667	2.91	AP-PA	2	930	617	51.3	36	31.4	29.2	27.6	26	24.2	21.2	33	478	335	292	272
1	3	19	2.94	14.3	2.85	2.93			2.3	2.69333	3.27	AP-PA	2	1204	991	58.4	38.9	31.3	28.1	26.2	24.6	22.9	20.5	28.5	704	467	377	339
1	3	19	1.12	14.4	3.28	2.87			2.22	2.79	3.48	AP-PA	2	888	635	52.1	35.8	29.8	27.1	25.3	23.7	21.6	18	25.9	461	318	264	241
1	4	22	1.36	14.5	3.21	2.92			2.27	2.8	3.52	AP-PA	2	643	658	49.8	35.5	31.3	29.1	27.2	25.3	22.9	18.1	30.6	321	228	201	187
1	3	28	1.91	14.6	3.31	2.79			3	3.03333	3.17	AP	1	879	930	51.9	38.1	33.5	30.9	28.8	26.8	23.9	18.6	33.4	457	334	294	272
1	4	21	3.64	14.6	2.72	1.35			2.64	2.23667	3.04	AP-PA	2	778	1070	52.7	39.2	33.7	30.8	28.8	27	25.1	22.7	35.1	409	304	261	240
1	4	25	1.86	14.7	2.45	2.14			2.22	2.27	2.65	AP-PA	2	777	958	50.2	35.4	29.4	26.6	24.8	23.1	21.2	18.2	24.3	391	275	229	207
1	4	23	1.75	14.7	3.82	3.22			2.3	3.11333	3.82	AP-PA	2	917	638	52	36.5	30.8	28	26.1	24.3	21.9	18	28.1	473	333	281	257
1	4	20	0.90	14.8	3.11	3.11			2.15	2.79	3.13	AP-PA	2	1039	654	55.7	38.4	31.3	28.4	26.4	24.6	22.4	18.6	28.8	580	399	326	295
1	5	25	1.90	14.8	3.3	2.8			2.26	2.78667	3.4	AP-PA	2	885	951	52.7	37.6	32.4	29.8	27.7	25.7	23.6	20.6	31.8	466	332	287	264
1	5	18	0.33	14.9	2.82	1.41			2.24	2.15667	3.2	AP-PA	2	693	909	40.2	27.9	23.7	21.1	19	17	15	12.4	13	278	193	164	147
1	4	25	1.66	14.9	2.58	2.3			2.99	2.62333	3.38	AP-PA	2	826	969	48.2	34.4	29.7	27.3	25.5	23.8	21.9	18.2	26.5	399	284	245	226
1	4	23	2.04	14.9	2.56	2.91			2.53	2.66667	3.08	AP-PA	2	1013	837	46.9	32.7	28.4	26.4	24.8	23.3	21.7	18.9	24.2	474	331	288	267
1	4	18	2.76	15.1	2.34	2.25			2.43	2.34	2.62	AP-PA	2	976	719	44.2	29.1	23.5	20.9	19.3	17.7	16.1	13.4	13.1	430	285	230	205

INCL	CT to R1	FU	mc	Apical	LL	CLD	ILD	SLD	AVG	MAX_LD	SCL	TRT	scitrt	VOL_Rx	Vol_opi	V5_SCL	V10_SCL	V15_SCL	V20_SCL	V25_SCL	V30_SCL	V35_SCL	V40_SCL	D25_SCL	V5CC_SCL	V10CC_SCL	V15CC_SCL	V20CC_SCL	
1	4	24	1.48	15.1	3.07	2.86			2.74	2.89	3.57	AP		1	951	718	50.6	34.9	30.4	28.1	26.4	24.8	22.8	19.4	29.3	480	332	289	267
1	6	20	1.37	15.2	2.45	2.85			2.08	2.46	3.29	AP-PA		2	827	702	49.5	35.6	30.9	28.5	26.7	25	22.9	19	30	411	295	256	236
1	5	21	1.83	15.2	2.68	3.12			3.34	3.04667	3.34	AP-PA		2	997	757	55.8	39.9	34.4	31.8	29.9	28.1	25.9	21.3	36.3	557	399	343	317
1	4	19	1.90	15.3	3.12	1.67			3.17	2.65333	3.65	AP-PA		2	973	1152	56	38.9	32.5	29.5	27.2	25	22.6	17.9	30.2	546	379	316	287
1	5	19	2.73	15.4	2.27	2.67			2.15	2.36333	2.8	AP-PA		2	1007	728	51.2	37.1	31.5	28.9	27.1	25.5	23.7	20.9	31.4	517	374	317	291
1	4	23	1.85	15.5	2.95	2.12			2.96	2.67667	3.37	AP-PA		2	824	897	50.8	36.2	31.3	28.9	27.1	25.4	23.4	20	31.2	418	298	258	238
1	4	22	2.92	15.5	3	2.7			1.93	2.54333	3.27	AP-PA		2	1248	1224	46.7	32.5	28	25.7	24.1	22.5	20.5	17.1	22.1	583	406	350	321
1	4	22	1.76	15.6	3.05	2.74			2.16	2.65	3.14	AP-PA		2	949	1115	52.5	36.4	31.2	28.8	27.1	25.5	23.5	20	31.3	499	345	296	273
1	4	22	1.28	15.8	2.92	2.95			2.08	2.65	3.11	AP-PA		2	1023	767	48.1	31.4	25.7	23.3	21.6	20.2	18.6	16.1	16.1	490	321	263	238
1	4	21	1.39	15.8	5.07	2.96			2.31	3.44667	5.27	AP-PA		2	940	1011	51.6	38.3	33.4	30.8	28.7	26.4	23.9	20.2	33	486	360	314	290
1	6	22	1.74	15.9	3.1	3.08			2.61	2.93	3.32	AP-PA		2	1067	919	43.4	31.8	27.9	25.9	24.4	22.9	20.9	17.3	22.8	463	339	298	276
1	4	20	0.77	16	3.61	2.98			3.37	3.32	3.82	AP-PA		2	922	1121	54.4	38.3	32.1	29	26.8	24.7	22.7	20.2	29.2	506	353	296	268
1	5	21	1.21	16.1	3.77	3.82			2.83	3.47333	4.54	AP		1	1181	963	53.7	39.1	32.9	30.1	28	26	23.9	20.7	32.5	636	464	389	356
1	4	19	1.92	16.1	2.54	2.12			2.15	2.27	2.81	AP-PA		2	1039	1146	54.4	39.6	33.5	30.3	27.9	25.6	23	19	31.2	566	412	349	315
1	4	25	2.24	16.1	2.51	2.26			1.67	2.14667	2.97	AP-PA		2	896	960	40.7	26.8	23	21	19.5	18	16.3	13.6	23.2	364	240	206	188
1	4	22	2.67	16.1	4.57	2.94			2.33	3.28	3	AP-PA		2	1034	780	56	38	31	28.4	26.5	24.8	22.7	19.2	29.2	576	391	324	294
1	4	20	3.10	16.2	2.24	2.37			2	2.20333	2.6	AP-PA		2	1149	840	48.8	36.1	31.5	29	27.2	25.3	23	18.7	30.7	559	415	361	334
1	4	23	0.74	16.3	2.96	2.38			2.35	2.56333	3.26	AP-PA		2	1031	691	53.8	36.2	30	27	24.9	23	20.9	17.7	24.7	553	372	309	279
1	4	19	2.43	16.7	3.12	3.33			3.13	3.19333	3.97	AP-PA		2	1002	1349	51.3	37.9	33	30.6	28.7	26.9	24.6	20.1	34.3	512	380	330	307
1	4	24	3.20	16.8	2.85	2.8			2.5	2.71667	3	AP-PA		2	1340	1142	45.5	34.2	30.4	28.4	26.8	25.3	23.5	20.4	31.1	609	457	406	380
1	5	23	2.98	16.9	2.86	2.75			2.34	2.65	2.88	AP-PA		2	1004	918	48.8	37.5	33.4	31.3	29.6	28	26.1	22.8	37	491	376	335	314
1	4	20	1.87	17.1	3.39	3.35			2.57	3.10333	3.64	AP-PA		2	1170	1223	48.6	36	31.7	29.4	27.4	25.6	23.3	18.6	31.5	569	421	372	344
1	6	25	2.64	17.7	2.05	1.92			2.23	2.06667	2.29	AP		1	1003	474	40.5	28.6	25.1	23.1	21.5	19.8	17.9	15	15.17	408	288	252	232
1	4	25	2.22	17.8	2.38	2.63			2.35	2.45333	2.67	AP-PA		2	930	1117	50.5	32.7	27.6	25.1	23.3	21.7	19.9	17.2	20.3	468	305	257	234
1	4	25	3.15	19	2.25	2.48			2.08	2.27	2.49	AP-PA		2	1140	1388	52.3	35.4	29.3	26.8	25.1	23.6	21.8	18.9	25.4	600	430	336	306
1	4	24	2.11	20	2.76	3.31			1.82	2.63	3.42	AP-PA		2	1105	1341	53.8	38.7	33	30.2	28.3	26.4	24.3	20.6	33.6	596	427	364	334
1	4	31	0.07	10.5	2.29	2.9			2.71	2.63333	3.09	AP-PA		2	607	695	45.9	32.7	27.9	25.7	24.1	22.7	21.2	19.1	21.9	442	315	268	247
1	4	23	0.37	11.4	2.24	2.85			2.58	2.55667	3.19	AP		1	834	1061	41.6	28.7	24.9	22.9	21.5	20.2	18.7	16.1	14.8	317	218	189	174
1	5	23	0.37	11.5	2.29	2.93			2.3	2.50667	2.68	AP		1	807	576	42.8	29.1	23.8	21.3	19.5	18	16.3	13.4	13.5	394	268	219	196
1	4	15	0.68	11.7	3.57	2.87			2.22	2.88667	3.69	AP		1	828	837	52.7	37.9	33.8	31.5	29.7	27.8	25.8	23	36.7	496	357	318	297
1	4	27	0.70	11.7	3.5	2.92			2.27	2.89667	3.54	AP		1	904	704	50	36.4	32.5	30.2	28.2	26.1	24.2	21.5	33.06	460	329	293	272
1	4	30	0.80	11.8	2.86	2.79			3	2.88333	3.07	AP-PA		2	687	703	53.2	35.1	29.6	27.2	25.4	23.8	21.8	18.4	26.3	477	315	266	244
1	4	22	0.80	12.2	2.89	1.35			2.64	2.29333	2.89	AP-PA		2	1042	746	47	28.1	22	19.4	17.7	16.3	14.5	11.6	11.9	431	258	202	178
1	4	22	0.96	12.3	2.71	2.14			2.22	2.35667	3.1	AP-PA		2	941	1131	57.9	39.7	33.3	30.4	28.5	26.7	24.7	21.3	34.4	522	358	300	274
1	5	15	1.10	12.4	2.16	3.22			2.3	2.56	2.64	AP-PA		2	935	704	42.9	28.7	24.1	22	20.6	19.2	17.8	15.6	13.6	359	240	201	184
1	4	14	1.10	12.6	2.58	3.11			2.15	2.61333	3.28	AP		1	759	698	56.8	40.6	35.1	32.1	29.6	27.2	24.3	20	34.2	309	221	191	175
1	4	14	1.13	12.7	2.81	2.8			2.26	2.62333	3.07	AP		1	1006	725	53.7	37.6	32.7	30.3	28.6	26.8	24.7	20.4	34.3	395	277	241	223
1	4	30	1.14	13.2	2.12	1.41			2.24	1.92333	2.52	AP-PA		2	599	668	51	34.9	29.9	27.5	25.6	23.8	21.8	18.6	26.7	1	0	0	0
1	4	22	1.15	13.3	1.39	2.3			2.99	2.22667	2.47	AP-PA		2	469	633	39.3	23	18.9	16.8	15.1	13.5	11.8	9	8.7	548	321	264	234
1	4	14	1.15	13.3	2.87	3.37			2.26	2.83333	3.24	AP		1	693	865	45.1	31.9	27.3	25.1	23.5	22.1	20.2	17.6	20.3	565	400	342	315
1	5	15	1.16	13.4	2.94	2.54			1.51	2.33	3.19	AP-PA		2	1074	759	46	30.3	26	23.9	22.2	20.7	19	16.5	17	365	240	206	190
1	4	16	1.17	13.4	3.02	1.42			2.27	2.23667	3.19	AP-PA		2	666	825	42.8	31.3	28	26.1	24.3	22.6	20.8	17.9	22.9	460	336	301	280
1	4	18	1.17	13.4	3.2	2.9			1.92	2.67333	3.31	AP-PA		2	878	743	71.9	45.1	35	29.6	26.7	25	23.7	22.7	29.9	650	408	316	268
1	4	17	1.19	13.4	3.99	4.09			2.71	3.59667	4.1	AP		1	836	942	42.1	30.5	27.3	25.3	23.4	21.6	19.7	17.3	20.8	396	287	257	238
1	5	22	1.20	13.6	2.9	2.23			2.53	2.55333	3.93	AP-PA		2	909	1089	46.5	35	31.1	29	27.1	25.3	23.4	20.7	30.6	347	261	232	217
1	4	13	1.23	13.7	3.31	2.5			2.39	2.73333	3.46	AP		1	589	705	49.1	33.4	29.3	27	25.1	23.1	20.6	17.1	25	371	253	222	204
1	4	15	1.24	13.8	2.52	2.97			3.5	2.99667	2.99	AP		1	793	967	48	32.4	27.8	25.6	23.8	22.1	19.9	16.1	21.5	421	284	244	225
1	4	13	1.32	13.8	2.96	3			2.38	2.78	3.15	AP		1	1121	810	48.4	32.9	27.5	24.9	23	21.2	18.7	14.3	19.8	363	247	206	187
1	5	17	1.40	13.8	2.28	2.94			2.58	2.6	2.54	AP		1	942	754	45.4	32.5	27.8	25.5	23.8	22.3	20.6	17.8	21.2	312	223	191	175
1	4	21	1.40	13.8	3.03	3.15			1.83	2.67	3.17	AP		1	1140	1257	50.6	35.4	30	27.8	26.1	24.5	22.4	18.6	28.4	549	384	326	302
1	4	31	1.47	13.9	2.63	2.79			3	2.80667	3																		

INCL	CT to R1	FU	mc	Apical	LL	CLD	ILD	SLD	AVG	MAX_LD	SCL	TRT	scitrt	VOL_Rx	Vol_opi	V5_SCL	V10_SCL	V15_SCL	V20_SCL	V25_SCL	V30_SCL	V35_SCL	V40_SCL	D25_SCL	V5CC_SCL	V10CC_SCL	V15CC_SCL	V20CC_SCL
1	4	22	1.50	13.9	1.94	2.14		2.22	2.1	2.84	AP		1	560	643	51.9	37.2	32.6	30	27.9	25.8	23.1	18.6	31.7	549	393	345	317
1	4	16	1.52	13.9	2.74	3.22		2.3	2.75333	3.1	AP		1	1046	830	47.5	32.7	27.8	25.4	23.8	22.2	20.3	16.8	21.1	316	218	185	169
1	5	15	1.57	14	2.52	3.11		2.15	2.59333	2.75	AP		1	736	883	52.8	38	33.1	30.4	28.3	26.2	23.5	19.5	32.5	311	224	195	179
1	4	17	1.57	14	2.72	2.8		2.26	2.59333	3	AP		1	824	627	46.3	32.5	28.3	26.1	24.3	22.6	20.6	17.6	22.9	482	339	295	272
1	4	24	1.60	14	2.77	1.41		2.24	2.14	2.93	AP-PA		2	756	881	47.2	35.6	32.1	30	28.1	26	23	13.8	32.2	388	293	264	247
1	4	21	1.61	14.1	2.5	2.3		2.99	2.59667	3.4	AP-PA		2	750	1033	50.2	36.5	30.9	28	26	24.1	22	18.7	27.7	374	272	230	209
1	4	23	1.61	14.2	2.73	2.91		2.53	2.72333	3.01	AP		1	1071	1259	50.7	36.15	31.3	28.8	26.3	25	22.85	18.85	5.17	355	253	219	202
1	4	30	1.63	10.5	2.57	2.25		2.43	2.41667	3.47	AP		1	822	694	54.9	38.5	33.9	31.5	29.7	27.9	25.5	21.5	35.7	494	347	305	284
1	5	22	1.64	11.4	2.98	2.86		2.74	2.86	3.14	AP-PA		2	921	1143	48.4	34.2	30	27.9	26.2	24.7	23.1	20.7	29	449	317	278	259
1	4	23	1.64	11.5	3.04	2.85		2.08	2.65667	3.06	AP		1	761	580	50	36.3	32.2	29.8	27.8	25	20.9	11.3	30	374	271	241	223
1	4	20	1.65	11.7	2.07	3.12		3.34	2.84333	2.81	AP-PA		2	747	934	48.9	37.4	33	30.4	28.3	26.3	24.2	21.1	33.2	435	333	294	271
1	4	16	1.68	11.7	2.68	1.67		3.17	2.50667	2.93	AP		1	700	800	52.7	39.3	34.7	32.2	30	27.9	24.9	19.8	34.9	316	235	208	193
1	5	20	1.71	11.8	2.54	2.67		2.15	2.45333	2.68	AP-PA		2	651	776	50.1	37.2	32.4	29.8	27.4	25.3	22.9	19.2	30.4	344	255	222	204
1	5	16	1.75	12.2	2.29	2.12		2.96	2.45667	3	AP		1	927.5	593	44.2	33.8	30.4	28.5	26.9	25.3	23.4	20.4	30.9	306	234	211	198
1	5	20	1.80	12.3	2.42	2.7		1.93	2.35	2.96	AP		1	918	573	49.7	35.2	30.5	28.2	26.4	24.7	22.8	19.4	29.2	393	278	241	223
1	5	22	1.87	12.4	2.72	2.74		2.16	2.54	2.81	AP		1	1395	1062	46.2	33.3	29	26.8	25.2	23.7	22	19.6	25.7	407	294	256	236
1	5	29	1.92	12.6	2.75	2.95		2.08	2.59333	3.2	AP-PA		2	901	679	48.3	32.6	28	25.9	24.4	22.9	21.4	18.9	22.8	438	294	253	234
1	5	14	1.97	12.7	3.39	2.96		2.31	2.88667	3.81	AP		1	1057	1143	47.9	36.1	32.1	29.8	27.9	26	23.5	19	32.3	395	297	265	246
1	5	31	2.00	13.2	2.94	3.08		2.61	2.87667	3	AP-PA		2	966	766	52	37	32	29.8	25.4	26.3	24.6	21.9	34	755	537	465	433
1	5	22	2.00	13.3	3.2	2.98		3.37	3.18333	3.27	AP		1	888	1103	54.7	37.8	32.8	30.3	28.1	25.9	22.8	18.2	31.7	601	415	360	333
1	5	15	2.03	13.3	2.91	3.82		2.83	3.18667	3.4	AP-PA		2	882	1017	53.2	38.5	33.9	31.3	29.3	27.6	25.5	21.6	35.8	596	432	380	351
1	4	20	2.08	13.4	2.22	2.12		2.15	2.16333	3.14	AP		1	881	746	57.2	37.3	31.1	28.3	26.3	24.5	22.6	19.6	28.6	554	361	301	274
1	5	31	2.08	13.4	2.7	2.26		1.67	2.21	3.1	AP-PA		2	903	675	44.3	31.4	26.6	24.3	22.8	21.4	19.9	17.5	18.3	363	257	218	199
1	4	22	2.09	13.4	1.81	2.94		2.33	2.36	2.52	AP		1	699	797	50.5	35.2	30.2	27.6	25.6	23.5	20.5	14.8	26.4	488	340	292	267
1	5	20	2.09	13.4	3.54	2.37		2	2.63667	3.76	AP-PA		2	747	971	51.4	36.4	32.3	30.4	28.6	26.9	24.6	20	34.1	582	412	366	344
1	4	16	2.10	13.6	2.94	2.38		2.35	2.55667	3	AP		1	1098	1389	52	38.3	32.9	30.4	28.5	26.8	24.7	21.3	34.4	244	180	154	143
1	4	20	2.12	13.7	2.35	3.33		3.13	2.93667	2.52	AP-PA		2	717	753	53.4	38.3	32.6	29.9	27.9	26.2	24.1	20.5	32.9	457	327	279	256
1	4	22	2.12	13.8	2.54	2.8		2.5	2.61333	3.24	AP-PA		2	992	623	52.5	35.8	29.6	26.9	25	23.5	21.7	18.4	25.4	521	355	294	267
1	4	30	2.13	13.8	2.92	2.75		2.34	2.67	3.31	AP-PA		2	827	714	54.3	38.3	33.2	30.3	28	26	23.9	20.4	32.6	618	436	378	345
1	4	15	2.16	13.8	2.67	3.35		2.57	2.86333	2.87	AP		1	952	1161	44.7	30.9	26.5	24.3	22.8	21.3	19.2	16.5	18.1	406	281	241	221
1	5	14	2.18	13.8	2.37	1.92		2.23	2.17333	2.62	AP		1	745	878	51.6	37	32	29.4	27.4	25.4	22.5	16.7	30.8	289	207	179	165
1	5	22	2.18	13.9	2.47	2.63		2.35	2.48333	2.74	AP-PA		2	1085	775	50	33	27	24	22	20.8	18.6	14.7	19.2	540	368	298	267
1	4	22	2.32	13.9	2.63	2.48		2.08	2.39667	3.05	AP-PA		2	958	695	55.5	35	29	27	25	23.5	22	18	25	530	337	281	257
1	4	21	2.36	13.9	2.63	3.31		1.82	2.58667	2.87	AP		1	552	638	47.4	34.1	29.2	26.7	24.8	22.9	20.1	15.4	24.6	262	188	161	147
1	4	16	2.41	13.9	3.4	2.9		2.71	3.00333	3.4	AP		1	855	620	49.5	37	32.3	29.7	27.7	25.8	23.2	18.6	31.7	463	346	302	278
1	4	22	2.52	14	2.6	2.85		2.58	2.67667	2.85	AP		1	790	975	51.6	37.1	30.9	28	25.8	23.6	20.4	16.3	26.9	361	259	216	196
1	5	14	2.56	14	2.32	2.85		2.08	2.41667	3.57	AP		1	686	780	44.9	34.5	31.2	29.3	27.5	25.6	22.8	17.5	31.2	470	361	326	306
1	4	22	2.60	14	2.7	3.12		3.34	3.05333	2.8	AP-PA		2	1132	826	55.5	39.1	33.1	30.3	28.5	26.7	24.7	21	34.2	501	353	299	274
1	4	30	2.63	14.1	2.13	1.67		3.17	2.32333	2.87	AP		1	890	713	55.4	38.6	31.5	28.2	25.9	23.8	21.6	18.3	27.1	537	374	306	274
1	5	22	2.63	17.7	3.3	2.67		2.15	2.70667	3.44	AP		1	969	930	55.7	39.2	32.8	30.1	28.2	26.6	24.5	21.2	34	495	348	291	267
1	4	14	2.68	17.8	2.14	2.12		2.96	2.40667	2.98	AP		1	677	513	52.7	37.3	31.8	29.2	27	24.9	22.12	17.1	29.7	601	425	363	333
1	4	16	2.90	19	3.55	2.7		1.93	2.72667	3.55	AP		1	1452	1635	48.3	36.1	31.9	29.7	28	26.2	24.2	20.9	33.2	367	274	242	225
1	4	24	2.92	20	2.03	2.74		2.16	2.31	2.48	AP-PA		2	820	1053	48.6	34.3	28.8	26.2	24.1	22.1	19.8	16	22.9	521	367	308	281
1	6	21	3.00	10.5	3.1	2.95		2.08	2.71	3.14	AP		1	900	587	50.8	37.3	33.2	30.9	29	27.2	25.1	21.5	35.1	420	308	275	256
1	5	20	3.09	11.4	2.39	2.96		2.31	2.55333	2.8	AP		1	962	771	54.1	38.2	32.4	29.8	27.9	26.1	23.8	19.7	32.7	515	364	308	284
1	6	16	3.10	11.5	2.32	3.08		2.61	2.67	2.64	AP		1	825	669	56.6	39.3	31.9	28.8	26.6	24.5	21.1	14.1	28.9	569	395	321	290
1	4	22	3.11	11.7	3.17	2.26		1.67	2.36667	3.34	AP-PA		2	1139	830	52.8	38.9	33.1	30.3	28.3	26.5	24.6	21.2	34	379	279	237	217
1	4	20	3.14	11.7	2.05	2.94		2.33	2.44	2.45	AP		1	897	993	49	37.1	32.9	30.6	28.8	26.9	24.4	20.7	33.9	332	251	223	207
1	5	21	3.20	11.8	2.78	2.37		2	2.38333	2.93	AP-PA		2	970	1314	49.6	35.2	30.8	28.6	26.9	25.2	23.1	19.6	30.4	475	337	295	274
1	4	23	12.15	3	2.38	2.35	2.576667		3.12	3.2	AP		1	981	47.8	33.7	28.8	26.5	24.8	23.1	20.8	17.1	24.3	311	219	187	173	161

V25CC_SCL	V30CC_SCL	V35CC_SCL	V40CC_SCL	Min_SCL	max_SCL	mean_SCL	ADM_CT	ADM_RT	ADM_FU	OTHERS
195	183	168	144	0.56	50.44	15.99		0	0	0
213	198	179	142	0.21	49.1	12.85		0 0 COUGH GIVEN PRESCRIPTION		0 HAD B/L PEDAL EDEMA AT END OF CHEMO
151	139	125	100	0.37	48.71	11.89		0	0	0
154	143	126	91	0.55	50.23	13.01		0	0	0
193	179	163	132	0.38	49.39	12.34		0 0 UTI URI		0 HYPOTHYROID
260	244	225	189	0.40	52.74	15.94		0	0	0
196	183	166	131	0.44	49.68	13.97		0	0 1 BSO	
203	187	170	140	0.40	47.85	15.48		0	0	0 HYPOTHYROID/PSORIASIS
241	225	207	177	0.25	49.93	15.95		0	0	0
237	222	204	175	0.28	49.59	15.68		0 0 FEVER chest clear URTI		0
237	224	208	177	0.44	49.22	15.59		0	0 0 MARCH 2016 COUGH CXR NORMAL	
250	232	211	175	0.26	50.5	15.15		0	0	0
233	216	197	162	0.45	48.92	14.38		0	0	0 gastritis
247	230	209	171	0.35	49.16	15.08	0 UTI		0	0
244	230	214	186	0.43	49.47	15.29		0	0	0
273	253	228	184	0.33	50.12	15.12	0 NIDER TC 1500 UTI	1 FEBRILE NEUTROPENIA		0 DYSPEPSIA
285	264	239	197	0.32	48.43	14.97		0	0	0
218	202	181	142	0.56	48.62	13.87		0 0- uti afbrile neutropenia	0 bso	B/L Cervical ribs
201	183	163	127	0.47	48.87	15.06		0	0	0
218	202	184	152	0.37	50.34	15.81		0	0	0 HYPOTHYROID/WOUND GAPING,
159	148	136	117	0.59	49.74	15.58		0	0	0
242	226	206	171	0.17	48.63	12.51		0	0 1 HEAD ACHE ENT	
206	192	176	153	0.23	49.28	11.95		0	0	0
161	150	137	114	0.33	48.78	13.48	3 FEBRILE NEUTROPENIA		0	0 PHOTSENSITIVE DERMATITIS
255	238	219	191	0.30	49.99	16.00		0	0	0
314	295	272	225	0.39	48.25	15.07		0	0	0
187	173	157	130	0.64	49.67	12.75	1 LOOSE MOTIONS T C ;		0	
236	221	202	167	0.41	49.09	15.84		0	0	0 ANEMIA
210	194	174	141	0.39	48.52	12.65		0	0	0 ANEMIA
174	164	151	126	0.27	47.64	14.66		0	0	1 MRM+Total thyroidectomy(STN) latter TAH+BSO
247	231	211	177	0.58	50.34	15.79		0	0	0 IHD
203	191	177	154	0.31	48.74	15.48		0	0	0
182	170	157	134	0.59	48.31	13.99	1 JAUNDICE	0 DRY COUGH		0
240	225	209	185	0.51	48.92	14.94		0	0	0
217	197	177	146	0.32	50.09	15.22	1 LOOSE STOOL/VOMIT		0	0 EX OUTSIDE
190	177	163	142	0.27	48.52	15.72		0	0	0 HYPOTHYROID
256	242	225	197	0.44	48.91	15.22		0	0	0
315	296	275	247	0.49	52.52	15.78		0	0 0 BSO OS	old # clavicle. Head ache MRI brain lytic lesion frontal bone, for observation
224	210	192	160	0.30	48.52	14.15		0	0	0 One TEF chemo OS
175	163	147	116	0.64	49.75	14.68		0	0	0
254	235	211	162	0.51	51.32	15.39		0	0	0 interpectoral node, I1 - 8+1; I1 total 18+1
224	210	195	177	0.24	56.49	16.61		0 1 LCM	1 BSO	
192	180	165	141	0.37	50.69	14.28		0 1 SUGAR CONTROLE	LUNG METS WITH P HYPOTHYROID/dfs 20 MONTHS LUNG METS	
239	222	201	164	0.21	50.29	14.59	1 NEUTROPENIA	1 GIDDINESS		0
275	256	233	194	0.26	49.56	15.00		0	0 2 EX BIOPSY FOLLOV MAY 17 CA LEFT BREST	
245	227	209	183	0.61	51.3	15.51		0	0	0
132	117	104	86.1	0.32	49.48	11.15		0	0	0
211	197	181	150	0.42	47.7	14.00		0	0	0 Hypothyroid, seizures/POST hysterectomy
251	237	220	192	0.54	50.49	14.14		0	0	0
188	173	157	131	0.28	49.87	11.63		0	0	0

V25CC_SCL	V30CC_SCL	V35CC_SCL	V40CC_SCL	Min_SCL	max_SCL	mean_SCL	ADM_CT	ADM_RT	ADM_FU	OTHERS
251	236	217	185	0.55	50.13	14.87		0	0	0 URI PAC
221	207	190	157	0.43	47.04	14.45	1 FOR CHEMO		0	0 HYPOTHYROID/BRUGADA SUYNDROMR/1.5 YRS DFS LIVER/?BONE METS ZOMETA CAPICITABINE
298	280	258	212	0.60	49.25	16.16		0	0	0
265	244	220	174	0.31	48.44	14.96		0	0	0 ANEMIA
273	256	239	210	0.31	48.74	15.48		0	0	0
223	210	193	165	0.32	50.89	15.00		0	0	0
301	281	257	213	0.35	49.21	13.43		0	0	0
257	242	223	190	0.60	49.46	14.98		0	0	0
221	207	190	165	0.32	50.77	12.98		0	0	0
269	249	225	190	0.16	51.91	15.59		0	0	0
260	244	223	185	0.40	48.2	13.20		0	0	0 MENINGIOMA
247	228	209	186	0.38	53.53	15.82		0	0	0 Gap correction given
331	307	282	244	0.33	51.18	15.45	Admision for every cher		0	0 Bulky cervix for observation
290	266	239	200	0.34	48.6	15.34		0	0	0
174	161	146	123	0.46	51.21	11.65		0	0	0 HYPOTHYROID
274	257	235	199	0.32	50	15.05		0	0 BSO	
312	290	265	215	0.36	48.08	14.47		0	0	0 ANEMIA/Extensive DCIS
256	237	215	182	0.00	49.58	14.50		0	0	0
288	269	246	202	0.23	49.23	15.16		0	0	0 Cervical lymphadenitis ATT/Hysterectomy on 2/3/17- endometrial polyp
359	339	315	274	0.24	50.82	14.61		0	0	0
297	281	262	228	0.29	47.45	15.57		0	0	0
321	299	273	217	0.38	49.97	14.67	1 NON NEUTROPENIC FI		0	0 ANEMIA
215	199	180	150	0.42	49.78	12.17		0	0	0 hypothyroid, on ATT since 2 months
217	202	185	160	0.53	49.89	13.76		0	0 1BSO	
287	269	249	216	0.37	51.2	14.60		0	0	0
312	292	268	226	0.35	50.37	15.59		0 1 FEVER VOMITTING		0
232	218	204	184	0.34	53.3	14.00				
164	154	142	123	0.50	51	12.30				
180	166	150	123	0.37	47.7	11.60				
280	262	243	217	0.53	50.5	16.20				
255	237	219	195	0.55	50.56	15.57		0	0 1BSO	HBSAg +, anemia/BSO AT FU
228	213	196	165	0.57	49.7	14.60				
162	150	133	106	0.23	51.8	11.20				
257	241	223	192	0.49	50.5	16.20				
172	161	149	130	0.35	51.3	12.40				
161	148	132	109	0.60	47.6	16.00				
210	197	182	150	0.55	49	15.60				IHD
0	0	0	0	0.39	50	14.50				
211	188	165	126	0.47	48.8	9.80				
294	277	253	221	0.27	50.84	13.40				SHIZOPHRENIA
176	164	151	131	0.48	49	13.00				
261	243	223	192	0.38	49.9	13.40				
241	226	214	205	0.56	80	21.50				
220	203	185	163	0.51	51.5	13.30				
202	189	175	155	0.32	51.9	14.90				
190	175	156	129	0.71	50	14.10				
209	194	175	141	0.50	49.9	13.40				
173	159	140	107	0.36	48.5	13.10				
164	153	142	122	0.37	50.2	13.50				IBS
283	23	243	202	0.33	52.1	14.50				esophageal Sx 20 yrs back
204	189	168	134	0.50	51.5	13.80				
251	236	218	189	0.59	52.1	16.20				

V25CC_SCL	V30CC_SCL	V35CC_SCL	V40CC_S	Min_SCL	max_SCL	mean_SCL	ADM_CT	ADM_RT	ADM_FU	OTHERS
295	273	244	197	0.68	49.1	15.10				
159	148	135	112	0.63	50	13.50				
167	154	138	115	0.56	48.8	15.40				
253	235	215	183	0.69	48.5	13.70				
231	214	189	113	0.39	43.6	13.90				Hypothyroid
194	180	164	139	0.25	51.8	14.60				DOE, allergic rhinitis
184	175	160	132	0.07	12.33	0.33				
267	251	230	194	0.62	50.8	16.10				
243	229	214	192	0.51	55.1	15.40				
208	187	156	84	0.70	43.8	14.00				
252	234	215	188	0.38	49.8	15.30				
180	167	149	119	0.40	47.9	15.70				
188	174	157	132	0.44	48.8	14.90				Anemia
186	175	162	141	0.60	49.1	14.60				
209	23	180	153	0.50	51.9	14.80				Heart Sx RHD
222	209	194	173	0.37	51.7	14.40				RHD
220	207	193	170	0.45	50.76	14.20		0	0	0
230	214	194	157	0.31	50.9	14.80				
369	382	357	318	0.54	50.7	15.80				
309	284	250	200	0.64	52.1	15.40				
328	309	286	242	0.57	48.6	15.90				
255	237	219	190	0.78	50.4	15.60				
187	175	163	144	0.28	53.3	13.40				Anemia
247	227	198	143	0.45	48.3	13.90				
324	305	278	226	0.57	51.2	15.40				
134	126	116	100	0.41	49.9	15.60				
239	224	206	175	0.38	50.2	15.50				Anemia
248	233	215	183	0.32	50.4	14.40				HYPOTHYROID
319	296	272	232	0.76	50	15.70				
207	194	175	150	0.47	53.5	13.50				
153	142	126	94	0.70	49.4	14.90				
246	225	202	159	0.27	48.75	13.07				
240	224	206	174	0.53	47.9	14.55		0	0	C/L SCL DFS 1 year
137	126	111	85	0.26	50	13.60				
259	241	217	174	0.52	48.9	14.90				
180	165	143	114	0.30	52.1	14.60				PSORIASIS,OA
288	268	238	183	0.40	50.3	14.30				Anemia
257	241	223	190	0.57	49.1	15.80				
251	231	210	178	0.33	50.92	14.90				Hypothyroid
250	236	218	188	0.23	52.3	16.30				
308	284	252	195	0.74	49.2	15.00				
213	199	184	159	0.34	51.2	15.20				
258	237	212	171	0.37	49.5	13.50				
240	225	208	178	0.64	51.7	16.00				
266	248	227	188	0.50	49.5	15.30				Sx Rt Clavicle 3 yrs back
268	246	212	142	0.39	48.8	14.70				
203	190	176	152	0.24	48.8	15.40				HYPOTHYROID, DEPRESION
195	182	165	140	0.40	51.6	15.40				
258	241	221	188	0.47	50.6	14.80				
150	135	111	0.30	51.3	13.90					

UHID	name	INDEX	yr	crt	Area_A	Shadow_S	DISTORT_D
------	------	-------	----	-----	--------	----------	-----------





ASD	Sum	RTFROM	RTTO	side	SIDECODE	PRE_RX	PRERXCOD	PRE_RT
-----	-----	--------	------	------	----------	--------	----------	--------



PRERTCOD	1YRCODE	ADM_CT	ADM_RT	ADM_FU	Age	Ht	H2	Wt
----------	---------	--------	--------	--------	-----	----	----	----



BMI	smoking	husband	DM	Htn	BA	PTB	TRT_COMC	OTHERS
-----	---------	---------	----	-----	----	-----	----------	--------



T

N

HIST

Grade

Pt

Pn

LI





L1_TOT	LII	LII_TOT	LIII	LIII_TOT	TOT	TOT_REMCPNS	LVI
--------	-----	---------	------	----------	-----	-------------	-----



PNI	ER	PR	Her2	Ki	TRT	TD	TRT_TYPE	TYPE_CT
-----	----	----	------	----	-----	----	----------	---------



REMARKS	Rx	HT	FU	T	TB	NTCP	TS
---------	----	----	----	---	----	------	----

LIVER METS XELODA

8/10/2017

5/26/2017

5/28/2017

TBS

NTCP\_SCL crt

Apical\_LD LL

CLD

ILD

SLD

MAX\_LD



18.2      2.78      2.5      2.04      3.09

SCL\_TRT VOL\_Rx Vol\_opp V5\_SCL V10\_SCL V15\_SCL V20\_SCL V25\_SCL V30\_SCL



V35\_SCL V40\_SCL D25\_SCL V5CC\_SCL V10CC\_SCL V15CC\_SCL V20CC\_SCL V25CC\_SCL V30CC\_SCL



V35CC_SCL	V40CC_SCL	Min_SCL	max_SCL	mean_SCL	V5	V5CC	V10	V10CC
-----------	-----------	---------	---------	----------	----	------	-----	-------



V15

V15CC

V20

V20CC

V25

V25CC

V30

V30CC

V35





V35CC	V40	V40CC	D25	min	max	mean	R1	R2
-------	-----	-------	-----	-----	-----	------	----	----



R3

R4